THE IDENTIFICATION AND MEASUREMENT OF AUTISTIC FEATURES IN CHILDREN WITH OPTIC NERVE HYPOPLASIA, ISOLATED HYPOPITUITARISM AND VARYING COMBINATIONS OF SEPTO-OPTIC DYSPLASIA.

by

JAGJEET JUTLEY

A thesis submitted in the College of Life and Environmental Science

University of Birmingham

for the degree of

DOCTOR OF PHILOSOPHY

School of Psychology

College of Life and Environmental Science

The University of Birmingham

March 2010

ABSTRACT

Research studies have identified that some children with Septo Optic Dysplasia and Optic Nerve Hypoplasia demonstrate autistic phenomenology (Parr *et al.,* 2008; Ek *et al.*, 2005; Pring & Ockelford 2005; Bahar *et al.*, 2003). It was found in fifty-six children, aged between four to sixteen, with isolated Hypopituitarism, Septo Optic Dysplasia and Optic Nerve Hypoplasia, that the susceptibility to autistic disorders was closely related to children's degree of intellectual disability, and visual loss, but not their hormone deficiencies. Furthermore, sensory impairments, and Self Injurious Behaviours, were also reported in children with Septo Optic Dysplasia and Optic Nerve Hypoplasia, but in greater numbers in children who had greater levels of intellectual disability and visual loss.

The clinical relevance of these findings of the thesis is that all children with Septo Optic Dysplasia and Optic Nerve Hypoplasia should have their development closely monitored by paediatric services at the hospital they attend. Furthermore, not being able to isolate the impact of intellectual disability, from that of the impact of visual impairment makes it difficult to isolate the origin of autism in the blind. The study also raises the further possibility that intellectual disability and visual loss may have an accumulative effect to the severity of autistic disorders.

Most importantly, the thesis highlights the need for an appropriate assessment tool to screen and diagnose for autistic disorders in children with visual loss. Ultimately, this will aid in early diagnosis and facilitate access to appropriate educational interventions.

To Mum and Dad

Acknowledgments

I would like to thank Dr Gillian Harris and Dr Jeremy Kirk for their supervision, support and patience throughout my PhD. I am grateful to the charities, Focus Families, Look, The National Blind Children's Society and staff at the Birmingham Children's Hospital for assisting in the recruitment of children for the theses.

A special thank you, to the families and children who have made this PhD possible.

Finally, I would like to thank my friends and family. Thank you to my mum, dad, brother and sister for being so caring and supportive during my studies. Thank you dad, for giving me the passion for education, you truly inspired me to strive in life.

I would also like to thank Amy Barkham and Steve for your advice, friendship and company in "the broom cupboard" and the Mres and PhD ladies, Amy Cook, Helen, Anna and Jude for your continuing friendship and support during our PhDs. Thank you to Louise Dacre for being there since the age of five and "sticking with me", you have made this journey enjoyable and listened to my constant PhD conundrums. Also, thank you for blessing me with two amazing Godsons. A deep thank you to my dearest undergraduate University friends, Kajal, Saima and Naj, we may separated by hundreds or thousands of miles, but the emails, visits and calls about Saima's and my PhD have surely kept us entertained. I anticipate that there will be a sigh of relief from Kajal and Naj when reading this. I would also like to thank Dean and Laura for their friendship, support, and most importantly for keeping me sane during my write up process

Finally thank you, to the Birmingham Children's Hospital and the University of Birmingham for funding my PhD.

TABLE OF CONTENTS

LIST OF TABLES

CHAPTER TWO

CHAPTER THREE

CHAPTER FOUR

CHAPTER FIVE

CHPATER SIX

LIST OF FIGURES

CHAPTER ONE

THE IDENTIFICATION AND MEASUREMENT OF AUTISTIC FEATURES IN CHILDREN WITH OPTIC NERVE HYPOPLASIA, "ISOLATED" HYPOPITUITARISM AND VARYING COMBINATIONS OF SEPTO OPTIC DYSPLASIA.

INTRODUCTION

1.1 Background to the present thesis

During out-patient paediatric endocrine clinics at the Birmingham Children's Hospital, autistic type behaviours were frequently observed in children with the clinical conditions, "isolated" Hypopituitarism, Optic Nerve Hypoplasia, and varying combinations of the syndrome, Septo Optic Dysplasia.

For this reason, a comparison of these closely related clinical conditions was necessary in order to investigate these anecdotal reports systematically. It was anticipated, that the composition of the cohort would generate three different hypotheses about the source of autistic traits within this cohort of patients. Specifically, were the origins of children's autistic behaviours in the present clinical cohort due to their hormonal deficiencies, visual loss or their neurological impairments? To achieve this objective, the present thesis necessitated selecting an appropriate method to measure, and identify, autistic behaviours in a wide range of children, including children with impaired visual function and/or intellectual disabilities.

1.2 Introduction to the clinical cohort

Firstly, the condition, Optic Nerve Hypoplasia (ONH) arises due to an underdevelopment of the optic nerves, and is considered to be one of the three leading causes of visual impairment in children within the western world Children with Optic Nerve

Hypoplasia demonstrate a wide spectrum of visual function ranging from normal visual acuity to complete blindness (Lambert, Hoyt & Narahara, 1987).

Secondly, the condition Hypopituitarism occurs because of hormonal deficiencies of the anterior lobe of the pituitary gland (Gasparetto, Warszawaik, de Carvalho-Neto, Benites, Bruck & Antoniuk, 2003). When one of the six hormones of the pituitary gland is affected, the condition is commonly referred to as "isolated" Hypopituitarism (Rona & Tanner, 1977). However, some children with Hypopituitarism can demonstrate associated brain abnormalities and/or Optic Nerve Hypoplasia, and this varying combination of anomalies leads to the diagnosis of the syndrome, Septo Optic Dysplasia (SOD) or De Morsier's syndrome (Thomas *et al.*, 2001).

A visual impairment in children with Optic Nerve Hypoplasia and Septo Optic Dysplasia can lead to certain developmental sequelae, such as Autistic Spectrum Disorders. This has been documented by researchers, Bahar, Brody, McCann, Mendiola and Slott (2003); Ek, Fernell and Jacobson (2005); Garcia-Filion *et al.,* (2008); Haddad and Eugster (2005); Ockelford, Pring, Welch, and Treffert (2005) and Parr, Shaffer, Salt, and Dale (2008) However, methodological issues, and the added complexities of within group variability, have challenged research within this area so far (Pring, 2005).

1.2.1 Introduction to the Autistic Spectrum Disorders

Autism is characterised by qualitative impairments in communication, social interaction, and by restricted, repetitive, and stereotyped patterns of behaviours and interests (DSM-IV- R; APA, 2000; ICD-10; WHO, 1992). Difficulties in social interaction on a behavioural level manifest as a general lack of expressed socio-emotional reciprocity. Qualitative impairments in communication can result in a lack of, or complete absence of,

spoken language for the purpose of communication, and impairments in non-verbal overtures such as the use of gestures to aid in communication (Shinnar *et al.*, 2001).

The third characteristic, of a restricted range of behaviours, activities and interests, includes repetitive body movements and patterns of play which are often restricted and repetitive (Filipek *et al.*, 1999). In addition, to these three areas of impairment in children with autism, are associated behavioural impairments. These include developmental delays (Lockyer & Rutter, 1969), unusual sensory processing disorders (Rogers & Ozonoff, 2005), abnormalities in eating, drinking, sleeping, mood, and self-injurious behaviours (SIB) (Dominick, Davis, Lainhart, Tager-Flusberg, & Folstein, 2007).

Sensory processing disorders correlate strongly with restrictive, repetitive and stereotyped behaviours (Rogers, Hepburn, & Wehner, 2003). Sensory processing disorders result in a hypersensitivity, or hyposensitivity, to visual information, sounds, touch, taste, smell, vestibular, proprioceptive, and kinaesthetic inputs, and these impairments have been observed in individuals with autism, blindness, deafness and children with intellectual disabilities (Wing & Gould, 1979). In addition, self-injurious behaviours correlate strongly with restrictive, repetitive and stereotyped behaviours and they commonly occur in children with visual loss, intellectual disability and autistic disorders. (Bodfish *et al.*, 1995), Types of self-injurious behaviours include head banging, hand-biting, excessive self-rubbing and scratching.

1.3 Methodological issues of assessing autism in the blind

To date there is yet to be a systematic methodical framework to work within, or to work towards, to assess Autistic Spectrum Disorders within the visually impaired. So far, research has conceded that there is a lack of validated psychometric tools to use for the visually impaired (Dale, 2005). However, current attempts have been made to resolve this

issue, but are yet to be published (Dale & Salt, 2008). The difficulties that diagnostic assessments encounter are that they rely, heavily, upon functional vision to establish autistic traits in children. This makes it necessary to exclude or adapt certain aspects of most diagnostic instruments and this consequently modifies the psychometric properties of these instruments. Knowing this, Dale and Sonsken (2002) state that newer developmental tools can provide better support to clinical and research specialities because they have at least been standardised on a normative and neurologically impaired population. Furthermore, Dale and Sonsken (2002) state that the incorporation of a range of developmental tools, help to provide a complete clinical picture of the child, and may solve some of the methodological issues that researchers face.

1.4 Theoretical issues of the assessment of autism in the blind

Vision produces a stream of consistent and reliable information for children. This information helps an infant to identify objects, and people, and to develop and regulate their motor behaviours (Warren, 1994). Furthermore, it provides reference points for how the space around the infant is organised, and ultimately the relationship the infant has to their immediate surroundings (Fraiberg, 1977). Logically, a loss of vision would inevitably produce impairments in a child's social and communicative behaviours, because much of our information about our social world originates through vision.

To date, researchers remain divided on the nature and origin of autistic behaviours in the visually impaired. On one side, phenocopy theorists suggest that blindness has certain developmental consequences, which include autistic-like behaviours such as echolalia, pronominal reversal, and the delayed emergence of pretend play, all of which are common developmental features of children with visual impairments and autism (Fraiberg, 1977;

Perez-Pereira, & Conti-Ramsden, 1999). Therefore, phenocopy features are an antecedent of development delays due to visual loss. Thus, they are transient, as they improve over time and even further with the implementation of the appropriate behavioural interventions (Baron-Cohen, 2002).

To partially support this, Rutter *et al.,* (1999; 2002) identified "quasi" autistic features (i.e. surface similarities) in Romanian children who had endured extreme environmental deprivation in orphanages, prior to being adopted by U.K families. In most cases, the rate of autistic features progressively declined after adoption, which was attributed to the removal of children from their initial deprived environment. Rutter *et al.,* (1999) concluded that sensory and social deprivation resulted in transient autistic-like behaviours in a proportion of children. Although, a small percentage of autistic behaviours persisted in a few children, researchers were unable to deduce if organic brain abnormalities, or the experience of deprivation, resulted in the permanence of these autistic characteristics. Summing up this theory, Baron-Cohen (2002) states that autism in visually impaired children is a surface similarity, similar to those "quasi" autistic features observed in Romanian adoptees by Rutter *et al.,* (1999), and therefore, are not truly autistic in their origin.

On the other hand, "co-morbidity" theorists suggest that blindness and autism occur more commonly together than predicted because they share genetic and environmental antecedents (Chase, 1972; Chess, Fernandez & Korn, 1978; Keeler, 1958, and Rogers & Newhart-Larson, 1989). Furthermore, the high prevalence of intellectual disability, which is commonly co-morbid with Autism Spectrum Disorders (DSM-IV-R, 2000; ICD-10, 2000; Wing & Gould, 1979), and blindness (Rogers, 1996) may further amplify the predisposition and/or vulnerability to autistic phenomenology in children. Nevertheless, Hobson (2004) suggests that there is "not a clear boundary between blind children with autism and those with

autistic features" (Hobson, 2005; pg 15). Thus, the phenomenology of autistic like behaviours in children with severe visual impairments remains a perplexing issue for researchers in this area.

1.5 Aim of the present thesis

To date, no attempts have been made experimentally to investigate how one could differentiate between blind autistic children and blind children with autistic like behaviours. The present thesis will attempt to use appropriate methodologies, to identify patterns, and severity of autistic symptomology and its associated characteristics in children with "isolated" Hypopituitarism, Optic Nerve Hypoplasia and Septo Optic Dysplasia.

1.6 Overview of present thesis

The present thesis will be divided into six parts. Chapter Two will review the current literature available on each syndrome specifically; exploring the prevalence, aetiology, physical phenotype and behavioural characteristics of children with the clinical conditions. In addition to this, there will be an in-depth review of Autistic Spectrum Disorders, and this review will explore the prevalence, aetiology, and behavioural characteristics of children with the autistic disorders.

The empirical component of this thesis will start in Chapter Three, and it will consider the utilisation of an appropriate measure to use for the assessment of autistic behaviours in children with visual impairments and intellectual disability. Secondly, Chapter Four will begin to systematically assess the anecdotal reports of autistic behaviours reported in children with "isolated" Hypopituitarism, Optic Nerve Hypoplasia and Septo Optic Dysplasia during outpatient clinics at the Birmingham Children's Hospital.

Chapter Five and Chapter Six will measure the commonly associated impairments reported in children with autistic phenomenology, intellectual disability, and visual loss. Particularly, the relationship and reported differences between children's intelligence levels and their adaptive behaviours will be considered. The final empirical component of the thesis will examine the prevalence of restrictive, repetitive and stereotyped behaviours, sensory processing disorders and self-injurious behaviours in children with "isolated" Hypopituitarism, Optic Nerve Hypoplasia, and Septo Optic Dysplasia. Finally, Chapter Seven will present an overview of the literature which was reviewed, the findings of the experimental chapters of the thesis, the implications, future research suggestions, and a final overall discussion of the major findings of the thesis.

CHAPTER TWO

LITERATURE REVIEW

2.1 Aims of the literature review

Firstly, following an introduction to the endocrine system, this review will examine the three syndromes in question; isolated Hypopituitarism, Optic Nerve Hypoplasia (ONH) and Septo Optic Dysplasia (SOD). Secondly, to answer the primary objective of the thesis, the review will examine Autistic Spectrum Disorders with particular attention afforded to the aetiology and previous research conducted within this condition. The aim of the review is to identify the possible vulnerability traits that children may have to autistic type behaviours in the three named conditions. These ideas will be used to suggest a future framework for the aims and hypothesis for the empirical component of this thesis.

2.2 Introduction to the endocrine system

It is important to start with an introduction to the endocrine system, with the view that two of the syndromes in question include deficiencies in hormone production in their symptomatology. It is this system and its hormones which influence almost every cell, organ, and process in our bodies. The system is instrumental in regulating, growth and development, tissue function, and metabolism, as well as reproductive processes.

The endocrine system consists of the hypothalamus and endocrine glands, collectively referred to as the "neuroendocrine system". It uses hormones as specific messenger molecules that are synthesized and secreted by endocrine glands. These glands are ductless, so hormones are released directly into the bloodstream where they travel to target organs and elicit an appropriate effect. The endocrine glands are the pituitary gland, the pineal gland, the

thyroid gland, the thymus, the adrenal glands, the gonads and the pancreas. Sections 2.2.1-2.2.7 will discuss the role of the neuroendocrine system in more detail (Brook, 2001).

2.2.1 The hypothalamus

The hypothalamus is located immediately below the thalamus at the centre of the brain. The hypothalamus produces neurohormones: "hormone-releasing-hormones" which are sent to the pituitary gland. These hypothalamic hormones travel to the pituitary lobes by way of a special capillary system; the hypothalamic-hypophyseal portal system where they turn on, or inhibit, pituitary hormone synthesis (Brook, 2001)

2.2.2 The pituitary gland

The pituitary gland is the size of a pea and is located at the base of the brain. It is often referred to as the "master gland" and it is made up of two main components: the anterior and posterior lobes. The lobes of this gland are derived from different neural cells at the early stages of embryogenesis. The anterior pituitary or *adenohypophysis* is composed of cells that secrete protein hormones. The posterior pituitary or *neurohypophysis* is an extension of the hypothalamus, and releases and/or stores hormones secreted by the hypothalamus.

The anterior lobe of the pituitary gland produces six hormones in response to being turned on by their corresponding hormone releasing hormones, which have been sent via the blood stream from the hypothalamus. These hormones are the thyroid-stimulating hormone (TSH), growth hormone (GH), follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin (PRL) and the adrenocorticotropic hormone (ACTH). The following sections 2.2.1 – 2.2.5 will examine the effects each of the above hormones elicits in the body (Brook, 2001).

2.2.3 Thyroid gland and thyroid hormones (TSH)

The thyroid gland controls the regulation of metabolic rate through the secretion of the thyroid hormone, thyroxin in response to the thyroid-stimulating hormone (TSH) which is released from the anterior pituitary gland. The thyroid gland produces three hormones: thyroxine (T4), triodothyronine (T3) and calcitonin and is located at the front of the neck.

An underactive thyroid commonly referred to as "hypothyroidism" causes a low metabolic rate, confusion, cold intolerance, weight gain and lethargy. Alternatively, an overactive thyroid or "hyperthyroidism" causes an increase in metabolism, increase in temperature, nervousness, and fatigue and weight loss (Kasper & Harrison, 2005).

2.2.4 Growth Hormone (GH/Somatropin)

Growth hormone stimulates growth and helps to control blood sugar levels. GH also stimulates the production of insulin-like growth factor one (IGF-1) in the liver which has growth-stimulating effects on a wide variety of tissues which are shown in Figure One, (adapted from Rang, Dale & Ritter, 1999).

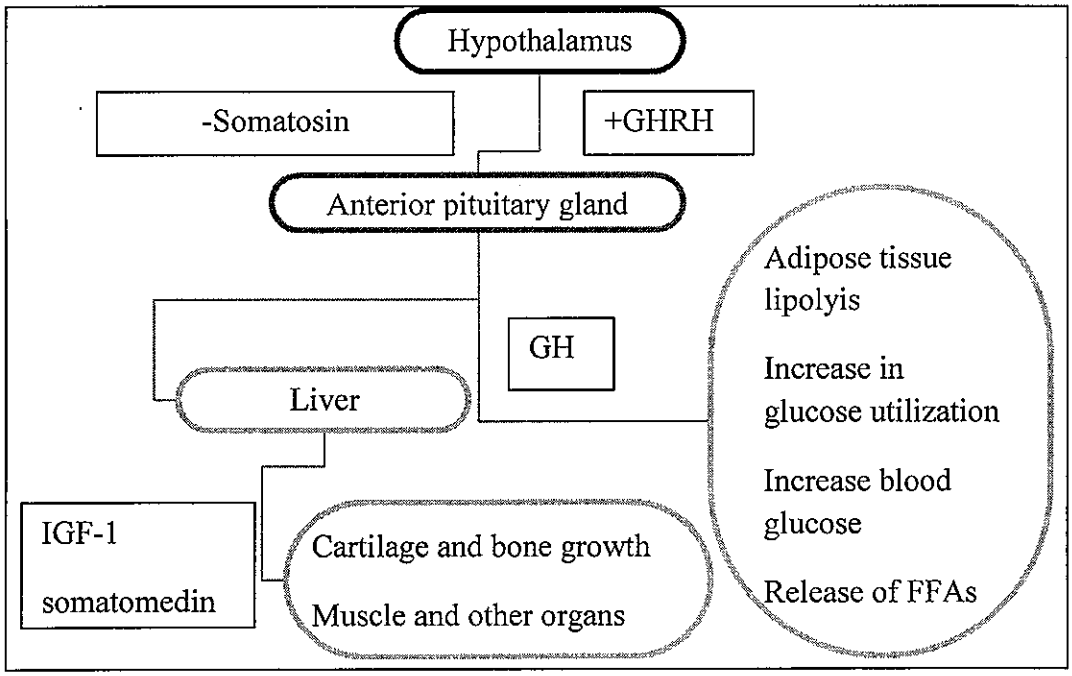


Figure One: GH role in development (adapted from Rang, Dale and Ritter, 1999)

As Figure One shows, IGF-1 helps to make chondrocytes, i.e. cartilage cells which make bones grow. Furthermore, when growth hormone binds to fat cells (adipocytes) it causes the breakdown of fats (triglycerides) in the body and blocks the body from holding on to, and storing, fats.

2.2.5. Luteinizing hormone (LH) and follicle-stimulating hormone (FSH)

These hormones start the cycle of puberty and are necessary for the development of fertility. Gonadtrophins are released by the pituitary gland after being stimulated by gonadtrophin releasing factors (GnRH) of the hypothalamus. Gonadtrophins send messages to the gonads to trigger the release of oestrogen in females and testosterone in males (Hadley, 2000).

Insufficient gonadtrophin production in young women, can lead to absence of menstrual cycles, infertility and loss of some female characteristics. Hormone replacement therapy of oestrogen is used to alleviate these symptoms. In men, this deficiency can lead to impotence, shrivelling of testes, decreased sperm production, infertility, and loss of some male characteristics. For young boys, hormone replacement therapy promotes puberty at a normal pace (Rang, Dale & Ritter, 1999).

2.2.6 Prolactin

This rare deficiency of the hormone prolactin causes an inability to produce breast milk after childbirth in some women. Prolactin deficiency is characterised by the inability of pituitary lactotrophs to secrete prolactin (Greenspan & Gardner, 2003).

2.2.7. Adrenocorticotropic hormone (ACTH) and Cortisol

The paraventricular nucleus of the hypothalamus synthesises and secretes vasopressin and corticotropin-releasing hormone (CRH). These two peptides regulate the stimulation and secretion of the adrenocorticotropic hormone (ACTH) by the pituitary gland. The hormone ACTH in turn, acts upon the adrenal cortices, which produce the glucocorticoid hormones, cortisol in response to stimulation by ACTH. These glucocorticoids act back on the hypothalamus and pituitary to suppress CRH and ACTH production in a negative feedback cycle. Cortisol is secreted in response to stress and cortisol levels affect blood pressure, the immune system and the heart (Greenspan & Gardner, 2003).

2.3 Isolated Hypopituitarism

Simmond first clinically described hypopituitarism, as a condition, in 1914 (cited in Masel, 2004) and over the last century, the definition of the condition has broadened to include a spectrum of hormonal deficiencies of the anterior or posterior pituitary gland (Toogood & Stewart 2008). The term "Hypopituitarism", describes a deficiency, or a complete loss of one or more of the hormones secreted by the pituitary gland. When a loss of all pituitary hormones occurs it is generally referred to as "panhypopituitarism", but a deficiency of one of the six hormones produced by the pituitary gland is referred to as a case of "isolated" Hypopituitarism (Geffner, 2002).

The severity, rate of loss and expressed manifestation of symptoms are dependent on which hormone is affected (Vance, 1993). For example, in Isolated Growth Hormone Deficiency (IGHD) a complete loss of growth hormone production leads to severe short stature, while an incomplete loss of growth hormone production results in insufficient levels of GH production to support normal growth velocity (Sizonenko *et al.*, 2001).

Additionally, growth hormone deficiency can occur alongside a deficiency of one or more of the other anterior pituitary hormones (Gonadtrophins, corticotrophin and thyrotrophic hormones). This occurrence is usually referred to as "Combined Pituitary Hormone Deficiency" (CPHD) (Vierira, Boldarine & Abucham, 2007) or Multiple Pituitary Hormone Deficiency (MPHD). MPHD also describes any combination of multiple hormonal losses.

The present thesis will discuss research, which explores cases of Hypopituitarism and specifically, isolated cases of growth hormone deficiency (IGHD), because approximately 50-70% of cases of Hypopituitarism are due to IGHD (Kirk & Butler, 2006).

2.3.1 Prevalence rates of Hypopituitarism

Incidence and prevalence of unspecific Hypopituitarism are estimated to be 4·2 per 100, 000 per year and 45·5 per 100, 000, respectively, in Spain (Regal, Paraamo, Seirra, & Garcia, 2001). Most commonly, GHD is the leading cause of short stature in endocrine disorders and accounts for 25% of cases (Kirk & Butler, 2006). Reported incidence rates vary between 1 in 3500-4000 (Stanhope, 2000) to 1 in 10, 000 live births for idiopathic cases of GHD (Lacey & Parkin, 1974; Rona & Tanner, 1977; Vimpani *et al.,* 1977, cited in Dattani, 2005). The syndrome also affects more boys than girls (Stanhope, 2000).

Within the U.K population, Traggiai and Tanner (2007) reported the incidence rate as 1 in 6, 00 live births. Furthermore, the National Institute of Clinical Excellence (NICE) in 2002 reported 2726 cases of IGHD in England, resulting in an annual incidence rate of 120 cases for the under sixteen population.

2.3.2 Aetiology of isolated Hypopituitarism

Hypopituitarism encompasses a group of different pathologies. When the condition is congenital, it is usually part of a larger syndrome such as Septo Optic Dysplasia, pituitary aplasia/hypoplasia or cleft palate disorders. It may also be acquired through tumours, infection or trauma (Geffner, 2002). Retrospectively, a higher incidence of breech births (Maghnie *et al.*, 1991; Triulzi *et al,* 1994), forceps delivery (Fujita *et al.* 1992; Fujisawa *et al.*, 1987; Kikuchi *et al.*, 1988) and vaginal bleeding has been documented during the birth of children with Hypopituitarism (Grossman *et al.,* 1983).

Overall, about 50-70%, cases of GHD still remain idiopathic, i.e. of unknown origin; but new laboratory techniques are now identifying genetic abnormalities. Genetic alterations in the production, regulation, secretion or bioactivity of GH have now been identified as causes of familial GHD in at least 5-30% of cases (Phillips & Cogan, 1994).

2.3.3 Genetic basis for the aetiology of isolated Hypopituitarism/IGHD

Four gene defects of the *GH* gene located on the arm of chromosome 17 (17q22-240) have been documented so far. Firstly, type IA IGHD shows an autosomal recessive pattern of inheritance resulting in the complete deletion of the *GH-1* gene. The phenotype expressed by type IA, is of severe short stature and intolerance to growth hormone treatment (Wagner, Eble, Hindmarsh & Mullis, 1998).

Secondly, children with the autosomal recessive IGHD type IB gene mutation show less severe short stature and a good response to growth hormone replacement therapy. Thirdly, children with IGHD Type II autosomal dominant inheritance pattern, display a milder form of short stature to other *GH* gene abnormalities. Lastly, children with IGHD type

III, an unknown X-linked recessive inheritance pattern, demonstrate short stature (Dattani, 2005).

Additional, heterozygous mutations of *PITX* (Suh, Gage, Drouin & Camper, 2003) *LHX3*, *LHX*, (Netchine *et al.*, 2000; Sheng *et al.*, 1996; Zhu & Rosenfeld, 2004) *PROP1* (Sornson *et al.*, 1996) and *POU1F1* (Mody, Brown & Parks, 2002) genes have been documented in mice models and humans. Six mutations of the *HESX1* gene during early embryonic development have been documented in cases of isolated, combined hormone deficiencies and the syndrome Septo Optic Dysplasia (SOD) (Carvalho *et al.*, 2003; Tajima *et al.* 1999; Thomas *et al.*, 2001; Thomas, Johnson, Rathjen & Rathjen, 1995), which all result in abnormal pituitary development. A more detailed review of the *HESX1* gene is examined in the genetics of Septo Optic Dysplasia section. In summary, the aetiology of isolated Hypopituitarism appears to be "multifactorial, with a combination of genetic and environmental factors" resulting in the expression of a diverse phenotype of hormonal deficiencies (Dattani, p.123, 2005).

2.3.4 Treatment of GHD

Growth hormone is available as biosynthetic growth hormone and is prepared by recombinant DNA technology. Historically, GH was extracted from cadavers until 1985 but was banned after the association with the viral infection, Jacob Creutzfeld Disease (CJD). As GH is a large protein molecule, it is injected into subcutaneous tissue or muscle daily (Geffner, 2002).

2.3.5 Physical phenotype of growth hormone deficiencies

A neonate with growth hormone insufficiency may present with hypoglycaemia and jaundice. Furthermore, boys may also present with hypogonodism and/or micropenis (Hadley, 2000). Diagnosis requires short stature; less than 2cm of growth in a year (on a standardised growth chart) and/or for at least one year, a slowing of growth velocity below the 25th percentile and delayed bone age. Untreated IGHD can lead to a final height range between 134-146cm in males and 128-134 cm in females. However, with GH treatment, height can increase by about 8.7-10.7cm in boys and 7.7-9.5 in girls (NICE, 2002).

A child with a growth hormone deficiency may present a distinct phenotype of normal body proportions, but an immature or cherub like face, small hands and/or feet. Skeletal abnormalities such as, protrusion of the frontal bones, poor development of the bridge of the nose and poor skeletal maturation are usually observed (Weinzimer *et al.,* 1997). Hypopituitarism is sometimes associated with diabetes mellitus, dyslipidaemia, cardiovascular complications (Clayton, 1998) and osteoporosis (Schneider *et al.*, 2007).

Growth hormone deficiency can also lead to diminished lean body mass and increased adiposal fat and truncal obesity. Presently, the charity "UK Child Growth Foundation" (2001) estimates that at least one third of children with IGHD are overweight. More systematically Beshyah *et al.,* (1995), Gotherstrom *et al.,* (2001), and Lonn *et al.,* (1993) found that, in their cohort of patients, all reported increased intra-abdominal fat. Beshyah *et al.*, (1994) attributed obesity in GHD patients to a reduction in protein, fat and carbohydrate metabolism.

For at least 50% of adolescents, with GHD, pubertal delays have been documented due to efficiencies in the luteinizing hormone and follicle-stimulating hormones. In addition, concurrent thyroid stimulating hormone and adrenocorticotopic hormones deficiencies occur

(UK Child Growth Foundation, 2001). Thus, IGHD symptomology can shift and evolve into a spectrum of deficiencies over time (Costin & Murphree, 1985).

2.3.6 Psychosocial phenotype of IGHD/Hypopituitarism

Few empirical research studies have been conducted on the behavioural consequences of hormone deficiencies. Research, which is available, has yielded conflicting evidence for the impact of hormone deficiencies on psychological development, although it is probable that being small for one's age may cause some social and psychological concerns. Problems with social skills that include attention deficits, shyness, and a deliberate withdrawal from friends and classmates have been reported (Stabler, Clopper, Siegel & Stoppani, 1994). However, other researchers have found that growth hormone deficiency does not impact on psychological wellbeing (Steinhausen & Stahnke, 1977) or a tendency towards depression or psychosomatic disorders (Frisch, Hausler, Linenbauer & Singer, 1990). In summary, emotional maturation of growth hormone deficient children can often be normal, but it can also vary widely (Law, 1987, Skuse 1972).

Looking at intelligence, a study of fifty two Ecuadorian children with a severe deficiency of insulin-like growth factor I (IGF-I) due to GH receptor deficiency, carried out by Kranzler, Arlan, Rosenbloom, Martinez and Guevara-Aguirre (1998), reported above average school performance in eighteen children with frequent hypoglycaemia or IGF-I dependence. In support, similar findings of higher intelligence levels in children IGF-I deficiency were reported by Gunnell, Miller, Rogers and Holly in 1995.

In contrast, Brown *et al.*, in 2004, using the Wechsler Intelligence Scale for children (WISC-III UK), assessed ten children with pituitary hormone deficiency (PHD). These children's conditions varied from isolated Hypopituitarism with normal MRI scans, through

to Septo-Optic Dysplasia and Multiple Pituitary Hormone Deficiency (MPHD). All patients were receiving hormone replacement therapy that included a daily injection of Growth Hormone.

The mean intelligence quotient score of children with hormone deficiencies was 75 (range 66-88) which was in the low range, when compared to the population norm of 100. Siblings had a mean intelligence quotient score of 82 (range 68- 108), however, intelligence quotient scores were not significantly different between the clinical group and their siblings. The clinical group did present significantly lower scores on the four subscales of perceptual organisation that include picture completion, picture arrangement, block design and object assembly.

2.3.7 Autism and Hypopituitarism

The social and communicative behaviours of children with IGHD/Hypopituitarism have yet to be systematically examined. What research is available is limited to case studies by Ragusa, Maurizio Elia and Scifo (1993) and Gingell, Parmar and Sungum-Paliwal (1996), who all described autism in children with Hypopituitarism. In addition, Gillberg, Gillberg and Kopp (1992) reported five cases of Autistic Spectrum Disorder in children with hypothyroidism. They suggested that hypothyroid hormone deficiency in early development resulted in brain damage or, alternatively, an autoimmune causation factor for the susceptibility for autism in these children.

2.3.8 Summary of Hypopituitarism

The degree of the deficiency varies greatly and depends upon the extent of the hormonal loss. As the endocrine system impacts upon many bodily processes it is inevitable

that such impairments may have an impact on a child's psychological processes. It is evident that prior research has not systematically explored the impact of hormone deficiency on a child's social and communicative behaviours. The following Section, 2.4, will discuss the second syndrome in question, Optic Nerve Hypoplasia (ONH) which can concurrently occur with Hypopituitarism.

2.4 Optic Nerve Hypoplasia

Optic Nerve Hypoplasia was first described in 1970 by both Walton and Robb and Edwards and Layden. Optic Nerve Hypoplasia is characterised by abnormal optic nerve axon development in utero resulting in various degrees of visual loss. (Mosier, Lieberman, Green & Knox, 1978; Fielder, Levene, Trounce & Tanner, 1986; Frisen & Holmegard, 1978; Mosier, Libermann, Lambert, Hoyt & Narahara, 1987; Whirney & Blodi, 1963). It was initially considered to be a rare non progressive congenital anomaly, but more recently is recognised as one of the leading causes of visual loss and blindness in children (Birkebaek *et al.*, 2003; Brodsky, 1991). In the USA, it is now one of the three leading causes of blindness (Steinkuller, Gilbert, Foster, Collins & Coart, 1999).

2.4.1 Aetiology of Optic Nerve Hypoplasia

The majority of cases of Optic Nerve Hypoplasia have an unknown aetiology, though four hypotheses have been explored. Deiner *et al.,* (1997) found that a failure of retinal ganglion cell axons to exit the optic disc occurred due to the netrin-1 molecule not guiding locally and Kallen, (2002) proposed that the pathogenesis of Optic Nerve Hypoplasia is related to an adverse event occurring during the development of the visual system in uetro.

Such an example would be stretching of the optic nerve during development of the cerebral hemispheres (Ellinberger & Runyan, 1970).

Further research has also shown that normal development of the retinal ganglion cells is followed by excessive pruning of the optic nerve (Zeki, 1990). Optic Nerve Hypoplasia is thought to occur due to a secondary dying back of retinal ganglion axons, which originally exited the optic disc into the optic nerve. Alternatively, Optic Nerve Hypoplasia can occur due to a basic failure of retinal ganglion cell differentiation during development (Brodsky, Baker & Hamed, 1996).

Genetic anomalies have rarely been documented (Awan, 1976; Mosier, Liberman, Green & Knox, 1978; Kytila & Neittinen, 1961), though several incidences of environmental and lifestyle choice of mothers have been implicated in the pathogenesis of this disorder. Maternal diabetes (Donahue, Lavina & Najjar, 2005; Foroozanm, 2005; Kim, Hoyt, Lessell & Sadun, 1986; Peterson & Walton, 1977), drug abuse (Chan, Fishmann & Egbert, 1978; Lambert *et al.*, 1987; McKinna, 1966) and maternal use of anti-epileptic drugs have all been documented in the aetiology of Optic Nerve Hypoplasia (Hoyt & Billson, 1978).

Researchers, Strömland and Pinazo-Durán (2002) compared ophthalmologic examinations of a group of Swedish children suffering from Foetal Alcohol Syndrome (FAS) (Strömland, 1985; 1987) and data from experimental rat models of FAS (Pinazo-Durán, 1993; Strömland & Pinazo-Durán, 1994). Interestingly, the most frequent finding of prenatal alcohol exposure was of damage to the retina and optic nerve of both humans and rats.

Further risk factors of low maternal age have been reported by Robinson and Conry (1986) and Margolith, Jan and McCormick (1977). To support this, Tze and Lapoimte (1984) reported that, in a cohort of mothers of children with Optic Nerve Hypoplasia, the mean maternal age of (22.1 years) was significantly different to that of a control group, (25.1 years).

Post-maturity has also been reported by Jan, Robinson, Kinnis and Macleod (1977) in a series of twenty cases of Optic Nerve Hypoplasia, 45 % of the clinical group were born after their due date and only one patient was born prematurely. In summary, the aetiology of Optic Nerve Hypoplasia also appears to be multi-factorial, though there is little genetic propensity to this syndrome.

2.4.2 Symptomology of Optic Nerve Hypoplasia

Children with Optic Nerve Hypoplasia demonstrate a wide spectrum of visual function, ranging from normal visual acuity to no light perception or complete blindness. A high percentage of children with Optic Nerve Hypoplasia have nystagmus (involuntary rhythmic movements of the eye) (Lambert *et al.*, 1977; Zeki, 1990), mild light intolerance (photophobia), and varying degrees of impairments in their perception of depth which increases in severity with increasing visual loss. More commonly, Optic Nerve Hypoplasia affects both eyes (bilateral) rather than one eye (unilateral) (Acers, 1981; Bilson, 1973), and it occurs equally in males and females (Zeki, 1990). During neonatal development, improvements in visual function can occur as a result of the maturation processes of the brain (Lambert *et al.*, 1987).

Around six in ten children with Optic Nerve Hypoplasia have additional hormone deficiencies (Kaufman, Kaufman, Borchert & Inlender, 2007), with the most prevalent being growth hormone insufficiency (Antonini, Grecco, Elias Moreira & Castro, 2002). In a cohort of forty-seven patients Ahmad *et al.*, (2006) reported that at least 71.7% presented with hormone deficiencies, of which 64.1% had a GHD.

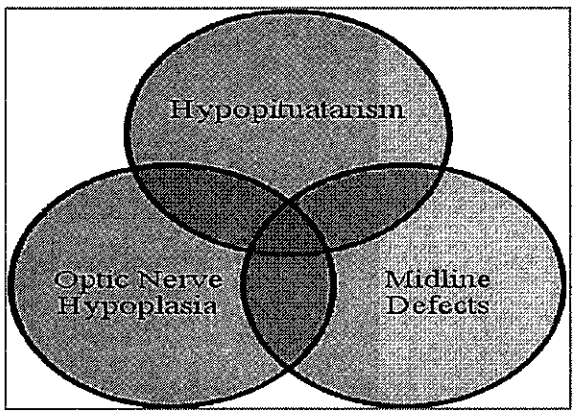
Frequently, bilateral cases of Optic Nerve Hypoplasia are more commonly associated with brain and endocrine abnormalities than are unilateral cases of Optic Nerve Hypoplasia

(Ouvrier, Lewis; Procopis, Billson, Slinik & De Silva 1981). When these additional symptoms co-occur with Optic Nerve Hypoplasia, children are usually diagnosed with the syndrome, Septo Optic Dysplasia (SOD). Due to the high association of Optic Nerve Hypoplasia with endocrine disorders and midline defects, much of the literature examines Optic Nerve Hypoplasia and Septo Optic Dysplasia synonymously. For these reasons, the following section, 2.5, will examine the third syndrome in question as well as aspects of Optic Nerve Hypoplasia.

2.5 Septo Optic Dysplasia

In 1956, De Morsier coined the term "Septo Optic Dysplasia" to describe a set of nine patients with an absent septum pellucidum and Optic Nerve Hypoplasia. Brook, Sanders and Hoare (1972) later described a further four cases of hypoplasia of the optic nerves, absent septum pellucidum, and endocrine abnormalities. A further three cases of pituitary dwarfism were also reported by Hoyt, Kaplan, Grumbach and Glaser in 1970.

Today, Septo Optic Dysplasia is described as a highly variable heterogeneous spectrum of disorders. For a child to be diagnosed, combinations of two or more of the following symptoms need to be present (1) hypothalamic-pituitary impairments, (2) Optic Nerve Hypoplasia (3) and/or agenesis of the midline brain structures, which includes the corpus callosum and/or septum pellucidum (Dattani, 1998). Figure two, below illustrates the heterogeneity and the possible varying severity patterns that patients may manifest.



Variability within each symptom

ONH = Blindness → normal vision

Midline Defect = severe → mild

Hypopituitarism = 1 to >1 hormone

Figure two: the spectrum and variability of the syndrome Septo Optic Dysplasia

2.5.1 Prevalence & epidemiology of SOD/ONH

Accurate prevalence figures are yet to be attained but the syndrome remains rare, and is thought to affect less than 2-6 in 100, 000 live births in Sweden (Blohme *et al.*, 1997). The National Institute of Health (NIH) reported that Septo Optic Dysplasia affects less than 200,000 people in the US population, and NORD, The National Organization for Rare Disorders, and Dattani and Robinson (2000) both presently put the prevalence rate at 1 in 50,000. The disorder affects an equal numbers of males and females.

More recently Patel *et al.,* (2006) extrapolated prevalence figures within the UK population by calculating the distribution of Septo Optic Dysplasia and Optic Nerve Hypoplasia in the Greater Manchester and Lancashire (GM&L) region of Northwest England. Eighty-seven cases had a confirmed diagnosis of ONH/SOD giving an incidence of 10.9/100,000 per year in GM&L which was much higher than previously reported figures. In addition, data from Patel and colleagues (2006) showed that high population density, inner-city locations, high rates of unemployment, dependent children in non-earning households, underage conceptions and underage pregnancies were all risk factors for the susceptibility to SOD/ONH. From these observations Patel *et al.*, (2006) concluded that environmental

exposure and lifestyle choices increased the susceptibility to Septo Optic Dysplasia and Optic Nerve Hypoplasia.

2.5.2. Aetiology of Septo Optic Dysplasia and Optic Nerve Hypoplasia

The development of the forebrain occurs as early as the six week stage of embryonic development. At this point the development of the pituitary gland, optic nerve and midline structures occurs in the same region of the embryo; that is the anterior neural plate. If trauma does occur and affects this particular region at a critical time in development, this would explain the particular expression of the combination of symptoms which we see in Septo Optic Dysplasia patients (Lubinsky, 1997).

To test this hypothesis, Lubinsky (1997) proposed that Septo Optic Dysplasia occurs due a vascular disruption sequence. The hypophysis (anterior pituitary) forms by the seventh week and the optic nerve soon after, while the septum pellucidum dates from 15-21 weeks. These components also arise from different developmental processes and tissues. Embryologically, the optic nerve is surrounded and penetrated by a primitive vascular plexus and the chiasmatic plexus anastamoses with the infundibular. The septum pellucidum is susceptible to atrophy or destruction with pressure or stretching (Freide, 1989).

Previous reports of maternal drug abuse during pregnancy have been implicated in some cases of Septo Optic Dysplasia (Orrico *et al.,* 2002). Also, mothers with epilepsy are at an increased risk of having children with mild congenital abnormalities and especially mothers who use valproic acid in conjunction with other anticonvulsant drugs for their treatment of epilepsy (Dieterich *et al.,* 1980). For instance, McMahon and Braddock (2001) reported, as case study, a child with Septo Optic Dysplasia born to a mother who took depakote (valproic acid) throughout her pregnancy. Hoyt and Billson (1978) reported seven

cases of associated anticonvulsant use during pregnancy and Optic Nerve Hypoplasia. During early gestation, the use of tobacco, alcohol and drugs such as heroin and cocaine have been implicated with some cases of SOD (Hume *et al.,* 1994; Michaud, Mizrahi & Urich, 1981).

Furthermore, McNay *et al.,* (2006) reported an association with young maternal age and Septo Optic Dysplasia; 34% of Septo Optic Dysplasia patients were born to mothers less than twenty years and nine months. Murray, Paterson and Donalson (2005) in Scotland found that in twenty six patients with Septo Optic Dysplasia the mother's median maternal age was 21 years (range 16-41), which was significantly lower than the median maternal age for Scotland of 27.12 years (range 25.8-28.6).

2.5.3 Genetics of Septo Optic Dysplasia

Mutations of the gene locus 3p21.2-p21.1 caused by the transcription factor HESX1 have been previously associated with Septo Optic Dysplasia (Carvallo *et al.,* 2003; Cohen *et al.,* 2005; 2003; Dattani *et al.,* 1999; Dattani & Robinson, 2002; Thomas *et al.,* 2001, Rainbow *et al.,* 2005). *HESX/Hesx1* is essential for pituitary and forebrain development in both humans and mice (Thomas, Johnson, Rathjen & Rathjen, 1995). To date, only sporadic and rare incidences of the association between *HESX1* and Septo Optic Dysplasia have been documented (David *et al.,* 2007).

The study by Thomas *et al.,* (2001) scanned for HESX1 mutations in a total of 228 patients with isolated Hypopituitarism, combined Hypopituitarism, and Septo Optic Dysplasia. Three different heterozygous mutations were detected in individuals with relatively mild pituitary hypoplasia or Septo Optic Dysplasia. The authors hypothesized that the expression of *HESX1* in the forebrain and the later restriction of its expression to the

Rathe's pouch, accounted for the variability observed in the phenotype of patients with Septo Optic Dysplasia.

Previous screenings of the gene *HESX1,* only explored limited coding regions of the gene, and this may have accounted for the low rates of observed associations between HESX1 and Septo Optic Dysplasia. McNay *et al.,* (2006) employed a more in-depth screening process of this gene, in a total of 314 non familial patients with Septo Optic Dysplasia and 410 patients with Optic Nerve Hypoplasia, isolated pituitary dysfunction and midline defects. McNay *et al.,* (2006) reported that the overall incidence rate of *HESX1* mutations was less than 1% in this cohort of patients.

Benner *et al.,* (1990) and Wales and Quarrell (1996) have both reported familial occurrences of a brother and sister, both of whom had features of Septo Optic Dysplasia. Furthermore, Blethen and Weldon (1990) described Hypopituitarism and Septo- Optic Dysplasia in first cousins. These observations suggest a Mendelian (autosomal-recessive) type inheritance (Wales & Quarrell, 1996).

2.5.4 Clinical phenotype of SOD/ONH

The phenotype of Septo Optic Dysplasia is variable, with at least 62% of individuals affected with Hypopituitarism and 30% having all three heterogeneous characteristics of the syndrome (Thomas *et al.,* 2001). Pituitary dysfunction can include Panhypopituitarism or isolated GH, ACTH or ADH insufficiencies (Emerson *et al.,* 2003). Recently, Birkebaek *et al.,* (2003) reported that, from a group of 55 individuals with Optic Nerve Hypoplasia, at least 49% patients had an abnormal septum pellucidum and 64% had hypothalamic-pituitary axis abnormalities. Endocrine abnormalities were higher in patients with an abnormal septum pellucidum (56%) when compared to those with a normal septum pellucidum (39%). In

addition, Arslanian *et al.*, (1984), further documented growth hormone deficiencies in 88% of patients diagnosed with Septo Optic Dysplasia, of whom 56% had adrenocorticotropic hormone deficiencies and 19% were TSH deficient.

Willnow *et al.*, (2005) further confirmed the variability in Septo Optic Dysplasia in the visual function of eighteen patients, which varied from unilateral hypoplasia of the optic nerve in seven cases, to bilateral hypoplasia in eleven individuals. Evidence of midline defects were collated from retrospective analysis of sonographic, CT or MRI scans. Four patients had a cavum septum pellucidum, three patients had hypoplasia of the cerebellum, one aplasia of the corpus callosum and one patient had aplasia of the fornix. An empty sella, with or without an ectopic pituitary, was seen in four cases. Endocrine deficiencies were detected in eleven patients of which seven exhibited isolated GH deficiency or multiple Hypopituitarism. The mechanism of the hypothalamic/pituitary dysfunction associated with visual loss in Septo Optic Dysplasia can be explained by the proximity of the optic tracts to the hypothalamus (Willnow *et al.*, 1996).

2.5.5 Structural brain abnormalities of the septum pellucidum and/or the corpus callosum in Septo Optic Dysplasia

Frequently, the septum pellucidum and/or part or all of the corpus callosum is partially or completely absent. The septum pellucidum is a thin membrane, which separates the anterior horn of the lateral left and right ventricles of the brain and runs as a sheet from the corpus callosum to the fornix. Riedl *et al.*, (2008) examined the septum pellucidum (SP) appearance from MRI scans. Sixty-eight patients with Optic Nerve Hypoplasia were investigated for the presence of associated SP anomalies. Thirty patients had either complete (n = 22) or partial (n = 8) absence of the SP. Pituitary hormone deficiencies were present in

64% or 25% of the cases, respectively. Neurological symptoms did not occur in patients with SP remnants or unilateral Optic Nerve Hypoplasia.

Hippocampus abnormalities (43%) and falx abnormalities (17%) correlated significantly with neurological symptoms and developmental delay. Twelve patients with pituitary anomaly and Optic Nerve Hypoplasia, but normal SP, showed similar clinical and MRI features, and were classified as SOD-like. In conclusion, Riedl *et al.*, (2008) reported that unilateral Optic Nerve Hypoplasia and SP remnants were associated with a milder Septo Optic Dysplasia phenotype, and Hippocampus abnormalities and falx abnormalities constituted a more severe clinical disorder, irrespective of the SP appearance. They further concluded that their data supported the hypothesis of vascular disruption during embryogenesis for the aetiology of Septo Optic Dysplasia and Optic Nerve Hypoplasia.

The corpus callosum is a thick band of fibres located between the cerebral hemisphere that connects the left and right cerebral hemispheres, it aids the intercommunication between the two hemispheres and underpins higher level cognitive functions (Just *et al.,* 2006). Agenesis of the corpus callosum (ACC) can result in seizures, feeding problems, and delays in fine motor and gross motor milestones, developmental delays and hydrocephaly (Taylor & David, 1997). Agenesis of the corpus callosum is associated with psychiatric disorders, attention-deficit hyperactivity disorder (Hynd *et al.,* 1995) schizophrenia, (Revito *et al.,* 1988) and autism (David, Wacharasindhu & Lishman, 1993; Hardan, Minshew & Keshavan, 2000).

According to Barkovich, Fram and Norman (1989) the presence or absence of schizencephaly (abnormal slits, or clefts, in the cerebral hemispheres) can help to identify two sub-types of Septo Optic Dysplasia. An association with schizencephaly and an absence of the septum pellucidum and corpus callosum has been well documented in Septo Optic Dysplasia (Kuhn, Swenson & Youseff., 1993; Kuban, Teale & Wallman; Miller *et al.,* 2000;

Lau, Tam, Lam & Wood, 1993). The first group present with both Septo Optic Dysplasia and schizencephaly and show normal size ventricles, remnants of the septum pellucidum, seizures and a spectrum of visual impairments or no impairment at all. The second group have no schizencephaly but a complete absence of the septum pellucidum, ventriculomegaly and hypothalamic and pituitary dysfunction. Barkovich *et al.*, (1989) proposed that, during the 7th and 8th week of gestation, some sort of insult to the embryo or infection could explain the association between schizencephaly and Septo Optic Dysplasia.

2.5.6. Other associated symptomology

Other associated symptoms of Septo Optic Dysplasia include, hypotonia (low muscle tone), seizures, thermoregulatory problems, jaundice, intellectual disability, external female genitalia anomalies, micro-penis/small penis, precocious puberty, and short stature/dwarfism (Barkovich *et al.,* 1989; Miller *et al.,* 2000; Orrico *et al.,* 2002).

Stevens and Dobyns (2004) reported a case study of limb defects and, by reviewing previous literature, they found five similar cases. They concluded from these findings that there was evidence for a vascular pathogenesis of Septo Optic Dysplasia in some patients which could have lead to limb defects. Harrison *et al.,* (2004) also reported limb malformations, including syndactyly of several fingers and toes, hypoplastic digits, and ring constriction of at least one finger. Brodsky *et al.*, (1997) also demonstrated a greater risk of sudden death in individuals with Septo Optic Dysplasia.

2.5.7 Psychological, social and communicative impairments in children with SOD/ONH

In a retrospective study by Ruggieri *et al.,* (2006) 135 patients with Optic Nerve Hypoplasia were divided into three groups, according to their clinical manifestations: Group

one presented with Optic Nerve Hypoplasia and CNS deficits; but no endocrine deficits. Group two: ONH and endocrine deficits; but no CNS deficits and Group three: ONH, CNS defects and endocrine deficits.

The data indicated that 40% (54/135) had Septo Optic Dysplasia and, of these patients, 48.1% belonged to group one; 16.6% to group two, and 35.2% to group three. Intellectual disability was present in 66.6%, autism in 11.1%, epilepsy in 22.2% and cerebral palsy in 8% of the cohort. The structural anomalies of the CNS were predictive of learning disabilities and/or epilepsy. Furthermore, Nariai, (2000) reported psychomotor delays and autism in a single case study of a patient with Septo Optic Dysplasia. Polizzi , Pavone , Iannetti , Manfré and Ruggieri (2006) also reported eight children (4 males, 4 females; age 2 to 17 years) with Septo-Optic Dysplasia who manifested dysmorphic features and the spectrum of autism, facial hemangioma, and holoprosencephaly.

Most recently, Garcia-Filion, *et al.,* (2008) assessed a cohort of 73 patients diagnosed with Optic Nerve Hypoplasia of which 71% of experienced developmental delays by the age of five years. Corpus callosum hypoplasia and hypothyroidism were significantly associated with poor outcome in all of the developmental domains. Absence of the septum pellucidum was not associated with adverse development. Researchers have also reported attention deficit disorders in children with SOD/ONH (Leonhard, Phill-Ann & Tann Sinn, 2005).

2.5.8 Autism in children with Optic-Nerve Hypoplasia and Septo Optic Nerve Hypoplasia

The fundamental problem of assessing autistic disorders in children with Optic Nerve Hypoplasia and Septo Optic Nerve Hypoplasia is the uneven cognitive and behavioral profiles that children present, because of the differing degrees and combinations of associated hormonal loss, mid-line malformations and/or visual impairments. Research studies by Parr *et*

al., (2008), Ek *et al.*, (2005), Pring and Ockelford (2005), Bahar *et al.*, (2003), confirm a common co-occurrence of autism and Septo Optic Dysplasia and Optic Nerve Hypoplasia and Chapter Four will provide an in-depth review of this literature.

2.5.9 Section summary

The three syndromes of isolated Hypopituitarism, Optic Nerve Hypoplasia and Septo Optic Dysplasia can occur as a combination of symptoms or in isolation. Previous research has highlighted the incidence of developmental problems and specifically autism in the children with Septo-Optic Dysplasia and Optic Nerve Hypoplasia and only a few case reports of autism and isolated Hypopituitarism have been identified, though this has yet to be explored systematically in all three syndromes. Section 2.6 will examine the disorder autism in detail, prior to moving on to the empirical component of the thesis, which will explore the co-morbidity of autism and its associated behaviours in the three syndromes in question.

2.6. Introduction to Autistic Spectrum Disorders

Leo Kanner first described "Early infantile autism" as a specific condition in 1943, in his seminal paper "autistic disturbances of affective contact", from the clinical observations of eleven children. The eleven children, showed striking similarities in their behaviours, specifically, "limitations in spontaneous activity", an "inability to relate themselves in the ordinary way", but a "good relation to objects" and their "relation to people" was somewhat peculiar (Kanner, 1943, p.246). Verbally competent children demonstrated "islets of ability", especially in their memory of past events, names and patterns (Kanner & Eisenberg, 1956; cited in Happe, 1994a).

From these observations, Kanner concluded, that all eleven children possessed, an "innate inability" to form meaningful social relationships, and that the core behavioural features of autism were, "extreme autistic aloneness", an "anxiously obsessive desire for the preservation of sameness" and mutism, which appeared to be associated with low intellectual abilities (Kanner, 1943, p.242).

That following year, Hans Asperger, independently described detailed case reviews of four individuals with a similar symptomatology, to that reported by Kanner in 1943, but Asperger's also reported children's empathy and non-verbal communication. This included inappropriate facial expression, eye-gaze, and gestures. Even with these social impairments, children were high academic achievers, with an average to high intellectual functioning level. Asperger named the disorder "autistic psychopathy", which is now commonly referred to as Asperger syndrome (Asperger, 1940, cited in Happe, 1994a, p.11).

2.6.1. The Conceptualisation of Autism as a Triad of Impairments

In 1979, Wing and Gould corroborated the early case reports of Kanner (1943) and Asperger (1944), in a large epidemiological survey in London. As a result of the survey, conceptually autism became viewed as "triad" of impairments". The triad incorporated, (1) a qualitative impairment in reciprocal social interaction, (2) a qualitative impairment in verbal and non verbal communication, and (3) the presence of restrictive manifestations of repetitive motor mannerisms, object and/or activities which hinder imaginative play. Today, the triad of impairments is encapsulated in the DSM-IV (APA, 1994) and the ICD-10 (WHO, 1992), the diagnostic criteria used for the diagnosis of autistic disorders by Paediatric Clinicians, Psychiatrists and Clinical Psychologists. The triad of impairments is summarised in figure three.

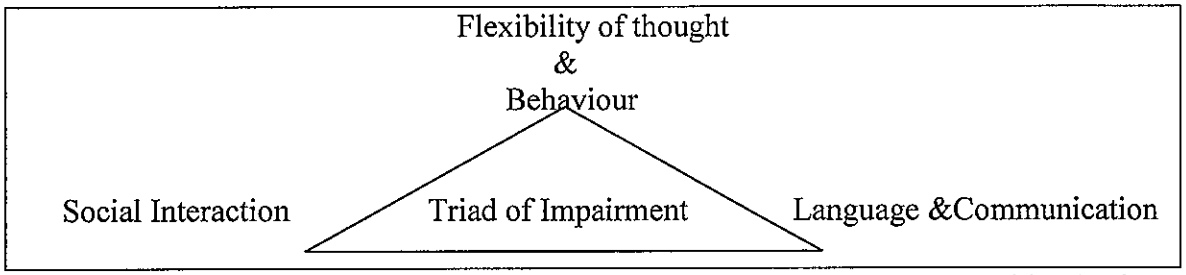


Figure Three: The triad of impairments observed in children with Autism Spectrum Disorders.

2.6.2 The diagnostic Classification System of Autistic Spectrum Disorders

Autism as a developmental disorder was only recognized in 1967 by the international classification of psychiatric disorders (ICD-8; WHO). In 1980, the term "Pervasive Developmental Disorders" (PDD) was introduced into the DSM- III (APA, 1980) to help categorise child developmental disorders into sub-groups. The current version of the DSM-IV (APA, 1994) and ICD-10 (WHO, 1992) includes autism, Asperger's syndrome, Pervasive Developmental Disorders- Not Otherwise Specified

(PDD-NOS), Childhood Disintegrative Disorder (CDD) and Rett syndrome, all under the umbrella term, PDD. Autistic Spectrum Disorder includes three of the five PDDs; autism, Asperger's syndrome and PDD-NOS.

2.6.2.1 The broadening behavioural phenotype of Autism Spectrum Disorder (ASD)

Since children demonstrated varying severities, and combinations of the triad of impairments, Wing and Gould (1979) coined the term "Autism Spectrum Disorder (ASD)" [1] to describe autism as a broad range of behaviours, with varying ability levels along a continuum. The main point in defining a spectrum was that, each manifestation of autism could occur in different degrees of severity, and in different combinations. As a result of this definition, the behavioural phenotype of autism has broadened over the years. Figure four, summarises the continuum of Autistic Spectrum Disorders.

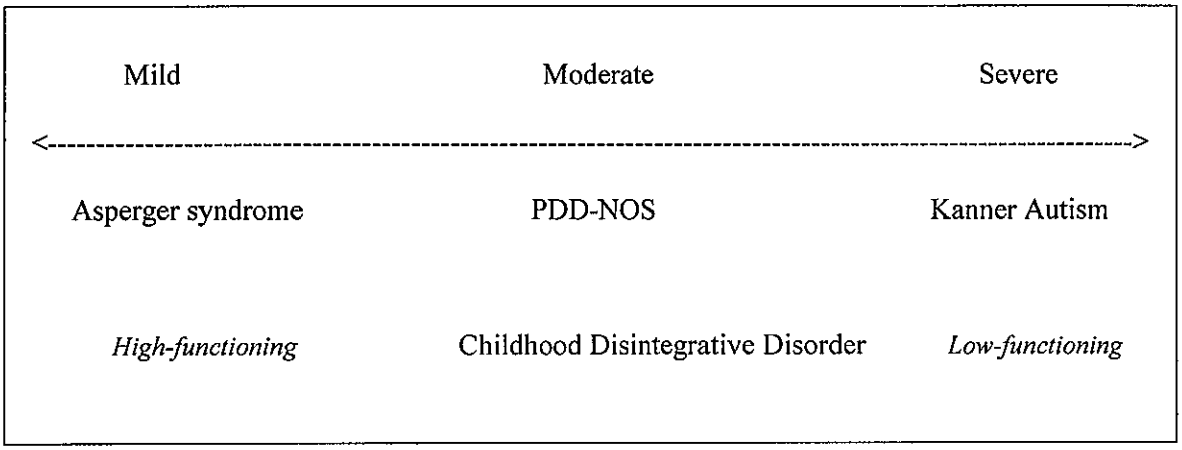


Figure Four: The severity of Autism Spectrum Disorders on a continuum

[1] *ASD will is used synonymously with the terms PDD, Autism, and Autistic Disorder throughout the thesis, as described in the DSM-IV. (1994).*

2.6.2.2 Differences between other Pervasive Developmental Disorders

Asperger's Syndrome, shares the features of autism, but delays in language or cognitive development which are commonly observed in children with autism are not required for diagnosis. Although, not part of the standard diagnostic criteria of the DSM (APA, 1994) or ICD-10 (WHO, 1992), motor clumsiness and atypical use of language are frequently reported in children with Asperger's Syndrome. The disorder, Pervasive Developmental Disorder Not Otherwise Specified (PDD-NOS), refers to a collection of behavioural features that resemble autism, but are not as severe or as extensive to warrant a diagnosis of autism from a Clinician.

2.7 Prevalence of Autistic Spectrum Disorders

The reported prevalence of autism has increased over the past thirty years (Kabot, *et al*, 2003). In 1979, the prevalence rate of childhood autism was considered to be as low as 4-5 per 10,000 births (Wing & Gould. 1979). Although, current research, suggests that the prevalence of autism is as high as 15-40 per 10, 000 births and Asperger's syndrome as 2.5 per 10,000 live births (Baird & Charman, 2002; Chakrabarti & Fombonne, 2001). Within the U.K, the Special Needs and Autism Project in London, reported prevalence rate of Autism Spectrum Disorders amongst children, as one percent (1 in 100 live births), (Baird *et al.,* 2006).

Explanations for this sizeable increase include better recognition amongst Clinicians and the public, the broadening diagnostic criteria of Autism Spectrum Disorders (Gernsbacher, Dawson, & Goldsmith, 2005; Rutter, 2005), better access to services for diagnosis, and the decreasing age of diagnosis (Fombonne, 2001; Howlin & Moore, 2001). Shattuck (2006), reported that the number of children in the United Kingdom diagnosed with `behaviour' and `developmental' disorders, but not autism,

tended to decrease by about 20% per between the years of 1992 to 2000, but the diagnosis of autism increased by 20% per year during this time period.

2.7.1 Age of diagnosis and onset of Autistic Spectrum Disorders

According to the diagnostic criteria outlined by the DSM-IV (APA, 1994), Autistic Spectrum Disorders can be reliably detected by the age of three years, and in some cases as early as eighteen months (Filipek *et al.*, 1999). Although, Howlin and Moore in 1997, cite the average age of diagnosis to be five years for autism, and eleven years for Asperger's syndrome. Delays in diagnosis are reported mostly amongst high functioning individuals and those with a severe intellectual disability.

Anecdotal parental reports, prior to diagnosis of Autistic Spectrum Disorders in their children, indicate that abnormalities in early development are often present during the first year of infancy. Initial parental concern about their child with autism has been reported amongst 30-50% of parents (Rogers & DiLalla, 1990). Abnormalities during the first year of infancy, included, poor eye contact (Gillberg *et al.*, 1990; Rogers & DiLalla, 1990; Volkmar, Stier, & Cohen, 1985), a lack of response to the parent's voices, and limited attempts to play or interact (De Giacomo & Fombonne, 1998; Gillberg *et al.*, 1990; Hoshino *et al.*, 1987; Rogers & DiLalla, 1990). Speech delays and stereotyped behaviour were often evident in the second year of infancy (Sullivan, Kelso & Stewart, 1990).

Similarly, several studies of early home videos have revealed behaviours indicative of autism in children later diagnosed with ASD compared to typically developing children (Adrien *et al.*, 1992; Adrien *et al.*, 1991; Baranek, 1999; Dawson, Osterling, & Dinno, 2000; Werner, Osterling & Dawson, 1994). During the first year of life, children with autism are distinguished by reduced social interaction (Adrien *et*

al.,1992), absence of social smiling (Adrien *et al.*, 1992), lack of facial expression (Adrien *et al.*,1992), failure to orient to name (Maestro, Casella, Milone, Muratori, & Palacio-Espasa, 1999; Mars, Mauk, & Dowrick, 1998; Osterling & Dawson, 1994), lack of pointing/showing (Mars *et al.*, 1998; Osterling & Dawson, 1994), decreased orienting to faces (Maestro *et al.*, 1999; Mars *et al.*, 1998; Osterling & Dawson, 1994), and a lack of spontaneous imitation (Mars *et al.*, 1998).

2.8 Core behavioural phenotype of Autistic Spectrum Disorders

As the aetiology of ASD is yet to be established, clinicians and researchers rely heavily upon observing children's patterns of behaviour for the diagnosis of ASD, according to the DSM-IV (APA, 1994) and ICD-10 (WHO, 1993) (Lord & Risi, 1998). For a diagnosis, the DSM- IV (APA, 1994) requires the presence of a total of six (or more) behaviours from the triad of impairments, with at least two impairments in the social interaction domain, and one each from the impairments in communication and repetitive and restrictive interest domain, all of which are discussed in the following subsections. Appendix one, provides a summary of the DSM-IV (APA, 1994) diagnostic criteria for all Pervasive Developmental Disorders.

2.8.1. Impairments in social interaction domain

Firstly, the DSM- IV (APA, 1994) requires at least two of the following behaviours to be exhibited by a child, in order for a diagnosis of ASD to be made from the domain of social interaction;

- Marked impairment in the use of multiple nonverbal behaviours, such as eye-to- eye gaze, facial expression, body postures, and gestures to regulate social interaction.
- Failure to develop peer relationships appropriate to developmental level.
- A lack of spontaneous seeking to share enjoyment, interests, or achievements with other people (e.g., by a lack of showing, bringing, or pointing out objects of interest).
- Lack of social or emotional reciprocity.

Impairments in social interactions are cardinal features of autism (Wing and Gould, 1979). One of the earliest indicators of autistic disorders in young infants is their lack of, or absence of joint attention abilities (Baron-Cohen, Allen & Gillberg, 1992; Charman *et al.*, 1998; Osterling & Dawson, 1994). Joint attention, describes a child's ability to integrate, and understand communicative social situations, which require interactions between the child, other individuals, and their environment (Jones & Carr, 2004). The emergence of conventional gestures, with gaze alterations and language, are all important skills needed to communicate effectively in social situations, which accordingly help a child make sense of their social world.

The first descriptions of the reduced incidences of joint attention skills in autistic children were described by Curcio (1978). Experimentally, Mundy, Sigman, Ungerer and Sherman (1986) used a "line of regard" task with children with autism and reported that children demonstrated a marked deficit in the capacity to follow, or understand the direction of an adult's gaze. During a further "referential looking" task, autistic children

showed impairments in looking back and forth between a person and objects, when compared to non-autistic children.

Another indicator of autistic children's impairments in social interaction is their failure to develop peer relationships, appropriate to their developmental age. Orsmond, Krauss and Seltzer (2004) assessed the prevalence of peer relationships in a sample of 407 autistic individuals using the Autism Diagnostic Interview – Revised, (ADI-R: Lord, Rutter & Le Couteur, 1994). Orsmond *et al.*, (2004) reported that only 8.1% of children had at least one peer relationship that was outside of a pre-arranged setting, 24.3% had a peer relationship within a pre-arranged setting, but 46.4% of individuals had no peer relationships, and this markedly differed to the pattern observed in children without Autistic Spectrum Disorders.

It has been also been reported, that children with autism display less positive, and more neutral affect, when compared to children with intellectual disability (Herzig, Snow, & Sherman, 1989; Loveland *et al.,* 1997). Moreover, Yirmiya and Shaked (2005) showed that children with Autistic Spectrum Disorders displayed a variety of ambiguous expressions and proposed that this unique pattern, may be related to impairments in sharing affect, and reading the affective signals of others.

In addition, Wing and Gould (1979) identified three types of impaired social interactions, commonly observed in children with Autistic Spectrum Disorders as social aloofness (with a neutral affect or indifference), passive interaction (does not initiate social interaction, but is not aversive to the approach of others), and active but odd interactions (initiates interaction which is odd).

2.8.2 Impairments in communication domain

Secondly, the DSM-IV (APA, 1994) requires a qualitative impairment in communication with the manifestation of at least one of the following symptoms listed below;

- Delay in, or a total lack of, the development of spoken language (not accompanied by an attempt to compensate through alternative modes of communication such as gesture or mime).
- In individuals with adequate speech, but marked impairment in the ability to initiate or sustain a conversation with others.
- Stereotyped and repetitive use of language or idiosyncratic language.
- Lack of varied, spontaneous make-believe play or social imitative play appropriate to developmental level.

A delay in, or lack of spoken language in children with autism is a cardinal feature of an impairment in communication. About 50-75 % of children with autism do not acquire useful speech, and those who do, may not use speech or non verbal speech as a means of communication (Rapin, 1991). Children who do acquire speech usually show a delay, with first words reported at thirty-eight months and phrase speech at fifty-two months (Howlin, 2003). Furthermore, the DSM-IV differentiates Asperger's syndrome from autism by the lack of, or delay in early language development. Eisenmajer *et al.*, (1998) found that language delay predicted autism in children younger than the age of six years.

Rapin (1991) argues that impairments in communication are more easily explained by an impairment of pragmatics. The term pragmatics refers to the way in which language is applied to social situations. Pragmatic language promotes the

initiation, contribution and choices of topic in conversation supported by non verbal cues of eye gaze, to and fro conversation and gestures.

To assess impairments in pragmatics in an ASD population Adachi *et al.*, (2004) compared high functioning PDD children (HFPDD) and children with attention deficit hyperactive disorder (ADHD) using the metaphoric and sarcastic scenario test (MSST). They found that HFPDD group performed poorer than the ADHD group in understanding sarcasm; however both groups found it just as difficult to understand metaphor.

The prevalence of pronominal reversal (e.g. saying "you" instead of "I" when referring to self) has been estimated by Rutter (1969) to be about 25% in children with ASD. It is also estimated that at least three-quarters of all verbal autistic children are echolalic (Frith, 2003). Prizant and Duchan (1981) refute the traditional notion that echolalia is meaningless, and view echolalia as serving many functions for a person with autism. They reported that immediate echolalia, was used for purposeful communication, and appeared to tap into the person's short-term memory for auditory input. Rutter (1966b) suggested that children, who do acquire language, usually go through a prolonged pre-echolalic stage.

Impairments in spontaneous make believe, or social imaginative play are early indicators of autistic phenomenology in infants. According to Boucher (1999) children progress through five stages of play; (1) sensory motor play (2) exploratory and manipulative play, (3) physical play including rough and tumble (4) social play and (5) make-believe play. In contrast, children with ASD spend much of their time in sensory play (Jordan & Libby, 1997) and manipulative play (Roeyers & Van Berckelaer-Onnes, 1994) and may not progress fully into the make believe stages of play.

Children with ASD have difficulties in the production of symbolic play when compared to children with Down's syndrome and typically developing children, and thus engage in less pretend play (Libby, Powell, Messer & Jordan., 1998). Roeyers and Van Berckelaer-Onnes (1994) described children with autism as missing the curiosity of typically developing children. They concluded that their play behaviours are often limited to simple manipulation and their quality of play, especially spontaneous and symbolic play, is more impoverished than that of non-autistic children of comparable mental age.

2.8.3 Repetitive and restrictive interest's domain

The final core feature of ASD is a restricted, repetitive, and stereotyped pattern of behaviour, interests, and activities. At least one of the following below needs to be exhibited for a diagnosis of ASD;

- Encompassing preoccupation with one or more stereotyped and restricted pattern of interest that is abnormal either in intensity or focus.
- Apparently inflexible adherence to specific, non-functional routines or rituals.
- Stereotyped and repetitive motor mannerisms (e.g., hand or finger flapping or twisting or complex whole-body movements)
- Persistent preoccupation with parts of objects

Stereotyped and restricted interests manifest in children with autism as rituals or routines that they feel compelled to perform. Some spend hours arranging objects in a certain way or insist on doing an activity in the same way. However, if their routine and ritual is interrupted, re-arranged, or moved this often results in extreme anxiety and distress (Frith, 2003).

Stereotyped behaviours are described by the DSM-IV (APA, 1994) as behaviours which are non-functional and driven. These behaviours often appear to be purposeless and invariant (Powell *et al.*, 1999). Repetitive Behaviours include repetitive motor stereotypes, narrow or circumscribed interests, compulsions, and severe problem behaviours, such as self-injury. Examples of motor stereotypy are hand flapping, body rocking, and/or spinning objects (Schreibman, Heyser, & Stahmer, 1999). Stereotypic behaviours are not isolated to autism as they are common to individuals with sensory, intellectual or developmental disabilities but are also common in typically developing children (Dykens, 2000). Rocking back and forth is reported in approximately 20% of typically developing children during early infancy (Kravitz & Boehm 1971; Sallustro & Atwell, 1978).

Repetitive Behaviours are prevalent in individuals with intellectual disability (Dykens, 2000), obsessive compulsive disorder (Leornard *et al.*, 1990), schizophrenia (Rocha *et al.,* 1996) and Tourettes Syndrome (Cath *et al.*, 2001). Restricted and stereotyped patterns of interest or the need for sameness can involve a persistent fixation on parts of objects or an inflexible adherence to specific, non functional routines or rituals. An in depth review of literature is discussed in Chapter Six.

2.8.4 Associated behaviours of Autism Spectrum Disorders

In addition to the primary characteristics of Autistic Spectrum Disorders, associated features are frequently observed. Abnormalities in unusual sensory responses, eating, mood, and self-injurious behaviours are frequently reported.

2.8.5 Impairments in Sensory Processing Disorders in children with Autistic Spectrum disorders

Early clinical reports of disturbances in sensory modulation (Kanner, 1943, Wing, 1969; Ornitz, 1977) and sensory processing impairments (De Myer, 1976; Rimland, 1990) have identified sensory dysfunctions as a central feature of Autistic Spectrum Disorders. Even with these early reports, unusual sensory experiences are considered only as an associated, but not essential feature, of autism by the DSM-IV (APA, 1994) and ICD-10 (WHO, 1992).

In spite of these early reports and clinical diagnostic endorsement, research within this area received little attention (Goldstein, 2000), until the 1980s, when high functioning adults with autism began to describe their personal experiences of their unique sensory world. Hypersensitivities to loud noises (Grandin, 2000), bright lights (Joliffe, Lansdown & Robinson, 1992), and difficulties in filtering out irrelevant information from the environment were described, resulting in a sensory "overload" in autistic adults. This often resulted in extreme anxious behaviours and confusion (Grandin & Sciarino, 1986). Sensory impairments result in a hypersensitivity, or hyposensitivity, to visual information, sounds, touch, taste, smell, vestibular, proprioceptive, and kinaesthetic inputs, which have been observed in individuals with autism, blindness, deafness and children with intellectual disabilities (Wing & Gould, 1979). Table 2.1, illustrates some of the commonly reported sensory impairments in children with Autistic Spectrum Disorder and an in depth review of literature is discussed in Chapter Six.

Table 2.1: common sensory processing impairments in autistic children

Hypersensitivity	Hyposensitivity
Hyperhearing (hearing the inaudible)	**Hypohearing (seeks sounds)**
• Responds negatively to unexpected or loud noises • Holds hands over ears • Makes repetitive sounds to block out other sounds (unable to "tune in")	• Bangs doors, objects • Likes crowds • Makes rhythmic sounds • Like vibration
Hypervision (seeing the invisible)	**Hypovision**
• Prefers to be in the dark • Avoids bright lights • Stares intensely at people or objects • Seeing "too well"	• Attracted to light • Looks intensely at object or people • Perimeter hugging • Concentrates on peripheral vision
Hypertaste/Hypersmell	**Hypotaste/smell**
• Avoids certain tastes/smells • Picky eater • Routinely smells non food objects • Seeks out certain tastes or smells	• Eats anything • Mouths and licks objects • Eats mixed foods (sweet and sour) • Seeks strong odours
Proprioception Hypersensitivity	**Proprioception Hyposensitivity**
• Continually seeks out all kinds of movement activities • Walks on toes/prances • Places body in strange positions	• Poor endurance • Rocks back and forth • Appears floppy, leans against people, objects
Vestibular Hypersensitivity	**Vestibular Hyposensitivity**
• Becomes anxious/distressed when feet leave the ground • Avoids climbing or jumping • Constantly seeking movement and this interferes with daily life	• Enjoys swings /Spinning • Runs around continually • Rocks back and forth • Bumps into people
Hypertactility	**Hypotactility**
• Avoids getting messy • Is sensitive to certain fabrics • Avoids going barefoot • Avoids people	• Touches people and objects • Decreased awareness of pain/temp • Hugs tightly • Prone to self injury

Adapted from Bogshima, 2003, pg 52-58)

2.8.6 Introduction to Self Injurious Behaviours

The term "challenging behaviour"; includes self injurious, aggressive, destructive, disruptive, socially undesirable and socially isolating behaviours. Common forms of Self Injurious Behaviours (SIB) include head-banging, hand-biting, and excessive self-rubbing and scratching. Self Injurious Behaviours are defined as; 'culturally abnormal behaviour(s) of such an intensity, frequency or duration that the physical safety of the person or others is likely to be placed in serious jeopardy' (Emerson 2001 p.1). There are many possible reasons why a person may engage in self-injurious behaviour, ranging from biochemical to social reasons. Aspects which influence self injurious behaviours include; internal factors such as medical/physical, cognitive/developmental impairments, communicative difficulties, social/emotional issues and external factors such as demands and environmental aspects (Emerson, 1992). Although influences can appear endless, all challenging behaviours have common elements; they are meaningful, relate to the needs and wants of a child, and are a means of communication and control. Such that a "child who has learnt to be violent has often learnt an effective way to control the environment, to gain attention, have needs met and avoid demands" (Jordan & Cornick 2000). A literature review of Self Injurious Behaviours is discussed in Chapter Six.

2.8.7 The co morbidity of autism with other neurodevelopmental disorders

The exact cause of autism remains unknown but recent research has found that specific medical conditions are highly associated with ASD. Celini, (2004) estimated that at least 24% of cases of autism are associated with other syndromes, with an infective, metabolic or genetic origin. Furthermore, at least 75% children with ASD have some form of intellectual disability. About 24% to 37% of cases of autism have

been attributed to biological or genetic defects such as, measles, Fragile X, Down's syndrome and Rett syndrome (Celini. 2004). Olsson, (1988), reported that 25% of children with epilepsy also had Autistic Spectrum Disorders, further emphasising the organic origin of the syndrome. Epilepsy is known to affect one third of children with autism by adulthood.

Individuals with Landau-Kleffner Syndrome also exhibit much autistic behaviour, such as social withdrawal, insistence on sameness, and language problems. William's Syndrome is characterized by several autistic behaviours including developmental and language delays, sound sensitivity, attention deficits, and social problems (Cellini, 2004).

However, most individuals with such syndromes have endured varying levels of biological and neurological damage so it becomes increasingly problematic to separate the behavioural phenotypes of such syndromes and those behavioural phenotypes reminiscent of Autistic Spectrum Disorders.

2.8.8 Intellectual disability and autism

Autism occurs at all intelligence levels, from high cognitive functioning levels to profound learning disability. Most individuals with an intellectual disability, show even skill development but, individuals with autism show uneven skill development (Lord & Volkmar, (2002). Children with intellectual disabilities and/or Autistic Spectrum Disorders, tend to a have a distinctive behavioural profile. For example, children with autism and intellectual disability show greater impairments in the Social domains of the Vineland Adaptive Behaviour Scale, compared to children with only an intellectual disability, who demonstrate lower scores across all sub-domains (Volkmar *et al.*, 1987).

2.8.9 The aetiology of Autistic Spectrum Disorders.

To date, there is no definitive biological, cognitive marker or medical diagnosis for Autistic Spectrum Disorders, and the disorder is diagnosed at a behavioural level. However, with the emergence of new brain imaging tools (e.g. Computerized Tomography (CT), Positron Emission Tomography (PET), and Magnetic Resonance Imaging (MRI), the biological basis of autism is continually being revealed. In addition, three neuro-cognitive theories of autism have emerged over the recent past, theory of mind deficit, weak central coherence, and executive dysfunction and such cognitive explanations provide an interface between brain and behaviour. Frith, Morton and Leslie (1991) have proposed a causative model of autism that encompasses both the genetic basis of autism and the behavioural manifestations in an autistic individual. Figure five, summarises Frith, Morton and Leslie's (1991) causative model of autism.

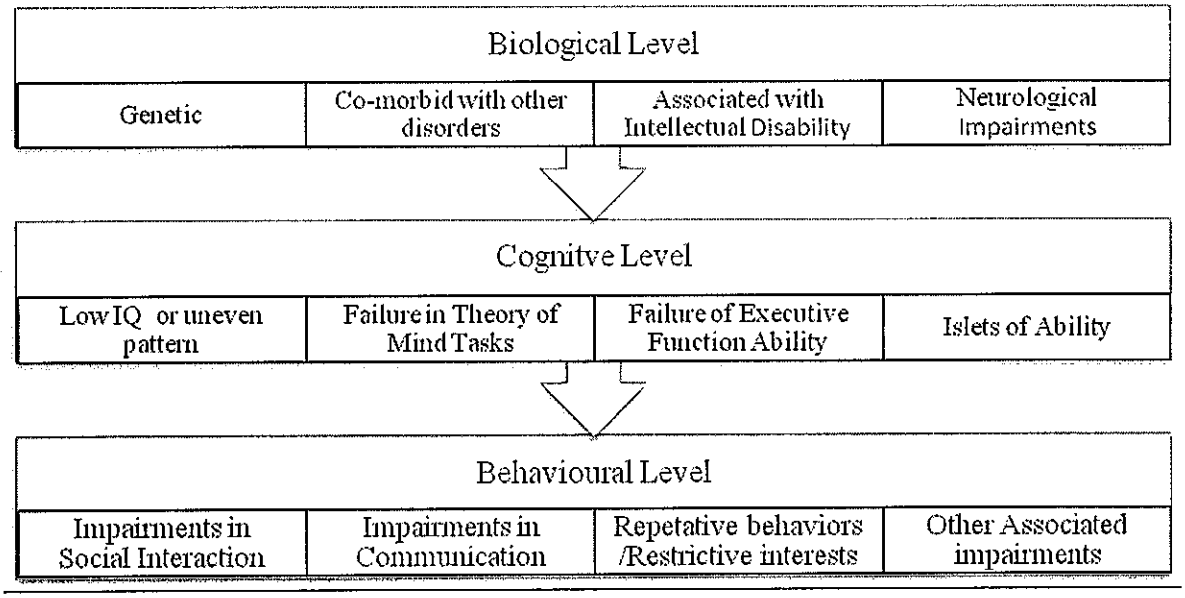


Figure Five: The relationship between the biological basis of autistic disorders, and its manifestation into explicit behaviours, through the intermittent impairment in cognition.

2.8.9.1 Neuroanatomical changes and Autistic Spectrum Disorders

Postmortem and MRI studies have shown that many major brain structures are implicated in Autistic Spectrum Disorders. These include the cerebellum, cerebral cortex, limbic system, corpus callosum, basal ganglia, and brain stem (Akshoomoff, Pierce & Courchesne, 2002). For example, Manes *et al.,* (1999) reported, smaller sized corpus callosum from the MRI scans of 27 low functioning autistic children, compared to seventeen aged matched children with an intellectual disability. In addition, Egaas *et al.,* (1995), Piven, Bailey, Ranson and Arnott, (1997), Harden, Minshew & Keshavan, (2000), Ritvo & Garber, (1988), Vidal *et al.,* (2003) have all reported a smaller sized corpus callosum in autistic children.

The largest MRI study of the cerebellur vermis using 200 patients with Autistic Spectrum Disorders reported an underdeveloped cerebellar vermis in children and adolescents (Hashimoto *et al.*, 1995). Furthermore, support for the role of the temporal lobe has been extrapolated from epileptic children; as in Autistic Spectrum Disorders the incidences of epilepsy is as high as 25% (APA, 1994). In addition, lesions of the tempro-frontal area, in herpes encephalitis, result in autistic symptomology in patients.

2.8.9.2 Genetics and Autistic Spectrum Disorders

Over the past two decades, family and twin studies have shown that genetic factors play important roles in idiopathic forms of Autistic Spectrum Disorders (Lamb *et al.*, 2000). Epidemiological studies, such as these carried out by Bailey *et al.*, (1995), reported that the probability of having both monozygotic twins with Autistic Spectrum Disorders was as high as 60%, but with dizygotic twins the probability was minimal. It is currently estimated that 2-6% of siblings of a child with autism also develop autism (Piven & Folstein 1994; Rutter *et al.*, 1999).

Looking closely at this genetic predisposition, the International Molecular Genetic Study of Autism Consortium (Barrett *et al.*, 1999; IMGSAC, 1999; Philippe *et al.*, 1999; Risch *et al.*, 1999) have all identified chromosomes 7p and 13p as possible susceptibility genes for ASD. Additionally, the IMGSAC, (1999) and Phillippe *et al.*, (1999) have also identified chromosome 1p, 16p and 19p as susceptibility genes.

A further unresolved puzzle concerns the fact that far more boys than girls develop autism. Two main explanations are being explored; firstly, that there may be a gene on the X chromosome that modifies the risk of developing autism (Skuse, 2000), girls possess two X-chromosomes (one inherited from the mother and the other from the father) whereas boys have just one (inherited from the mother), and this has led to speculations about X linked genes cause autism.

An alternative explanation is that sex hormone differences between boys and girls, rather than genetic differences, are responsible for the lower rate of autism (Lord & Schopler 1987). To support this, Ingudomnukul, Baron-Cohen, Wheelwright and Knickmeyer, (2007) undertook a study of foetal testosterone exposure and its effects on language and social abilities in children. The data showed that high foetal testosterone levels were associated with more social difficulties at school, and with narrow interests.

2.8.9.3 Pre- and peri-natal risk factors to autistic disorders

Prenatal exposure to exogenous substances during the first trimester may be an important in the development of Autistic Spectrum Disorders (Glasson *et al.*, 2004; Maimburg *et al.*, 2002). Exposure to legal and illegal drugs such as valporic acid, cocaine or alcohol has all been associated with Autistic Spectrum Disorders (Hultman *et al.*, 2002; Newschaffer *et al.*, 2002). Common to all these non genetic causes for Autistic Disorders, is an insult or disruption, at a critical period during the developmental process

in uetro (Hultman *et al.*, 2002) and this has also been suggested for the development of Septo Optic Dysplasia and Optic Nerve Hypoplasia (Lubinsky,1997). However, increased maternal age is strongly correlated with the Autistic Spectrum Disorders (Glasson *et al.,* 2004; Hultman *et al.*, 2002), and low maternal age is strongly implicated in the development of Septo Optic Dysplasia and Optic Nerve Hypoplasia (Patel *et al.*, 2006)

2.8.9.4 Cognitive explanations for Autistic Phenomenology

At their core, neurological changes to the brain, which result in Autistic Spectrum Disorders, translate at a behavioural level into complex social and cognitive deficits. Deviations in social behaviour and cognition have lead to several cognitive theories to explain the autistic phenomenology. The establishment of impairments in socialisation as a core feature of Autistic Spectrum Disorder, led psychologists to question whether higher cognitive abilities which governed the understanding of others minds, could explain some of the problems that children with Autistic Spectrum Disorders encountered.

2.8.9.5 Theory of Mind

The term, "Theory of Mind" was coined to describe a system of inferences which could not be explicitly observed, but could be used to make predictions about the behaviour of others. Through a series of experimental research studies, Baron- Cohen (2001) found that autistic children failure to see events from another person's perspective, i.e. understanding another person's mind.

During infancy, a child becomes aware of themselves and others as active agents in their social environment. The emergence of Theory of Mind (ToM) sets in motion an

understanding that people are mental beings, with their own beliefs, desires, emotions, and intentions (Wellan & Lagattuta, 2000). The primate research by Premack and Woodruff (1978) provided developmental psychologists, Wimmer and Perner (1983) with an experimental framework for conducting systematic research about the development of Theory of Mind in human children. They devised a set of stories called the "Maxi Task". Children observed two puppets, "Maxi and Mary", acting out a scenario using two containers, "a box and a basket". The story was acted out by Maxi who placed his toy in the basket, and then he left the stage. While Maxi was away, Mary moved the toy from the basket into the box, and she also left the stage. Maxi then returned and the child watching was asked a series of questions. Firstly, a "Prediction question; "Where will Maxi look for his toy first? Secondly a "Look question", where will Maxi think his toy is when he first comes in? Lastly, a "Think question", "Why do you think Maxi looked in the box?"

Wimmer and Perner (1983) reported that children aged four or under, tended to answer incorrectly that Maxi would look in the box (these children held a false- belief) while children older than four tended to answer correctly, that Maxi would look in the basket. They concluded that Theory of Mind was not completely acquired until children had undergone a shift in their thought processes and this, usually happened at around four years of age. The research also demonstrated that Theory of Mind had stage-like qualities in which children progressed only with age as the complexity of task increased.

2.8.9.6 Autism and Theory of Mind

Researchers began to question whether higher cognitive abilities which governed the acquisition of Theory of Mind, could explain some of the social problems that children with Autistic Spectrum Disorder encountered. Baron-Cohen, Leslie and Frith

(1985) used a simplified version of the Wimmer and Perner (1983), Maxi task to answer this question. Three groups of children; without developmental disabilities (control group), children with Down's syndrome and autistic children were compared on the Sally-Anne task. Most children with Down's syndrome, and the control group answered correctly that Sally would look in the box. However, most autistic children answered incorrectly that Sally would look in the basket.

The intelligence quotients of children with Autistic Spectrum Disorder was on average higher, when compared to the other groups of children, and so this indicated that the findings were not a result of lower intelligence, but due to children with Autistic Spectrum Disorders, not understanding that Sally had a "false-belief". Baron-Cohen, Leslie and Frith (1985) concluded that children with Autistic Spectrum Disorder were unable take Sally's perspective since they lacked a Theory of Mind. Furthermore, none of the autistic children could pass a second-order Theory of Mind task, which involved understanding what Anne thinks Mary thinks. The importance of Theory of Mind as an intrinsic and crucial modality for social development (Baron-Cohen, 1999) has been demonstrated through a number of studies summarised in table 2.2.

Table 2.2: Summary of Theory of Mind Research

Authors and Task	Task Description	Findings
Understanding What the Brain is For (Wellman & Estes, 1983).	Children were asked to identify mental functions (dreaming, wanting, and thinking) and physical functions (what makes you move or helps you stay alive).	Control: Three to four old children knew both physical and mental functions. Autistic children could on identify the physical functions of brain.
Appearance Reality Distinction, (Flavell, Green & Flavell, 1986)	When and why an object has a misleading appearance to what it is intended to be used for. For example, a candle shaped as an apple is shown to children. Children asked what is it?	Control: Three year olds and generally fail as they cannot hold both reality and appearance together. But by the age of six they can.
Seeing Leads to Knowing, (Pratt & Bryant, 1990; Baron-Cohen & Goodhart, 1994)	Character A looks in a box and character B touches the box. Children are asked who knows what is inside the box, character A or B	75% failed task of three year old failed the task
First-order false belief tasks, (Baron-Cohen, Leslie & Frith, 1985)	Sally-Anne Task	20% passed
Second-order false belief tasks (Baron-Cohen,1989b)	Involves embedded mental states	Controls passed at six years of age compared to nine years for high functioning ASD and Asperger Syndrome

2.8.9.7 Other Cognitive theories of Autistic Spectrum Disorders

Harris's simulation theory (1991) of the "self", postulated that children acquire an understanding of other's minds by using simulations of the self in the same situation. For example, children put themselves in the shoes of others, to make predictions, and explain the behaviours of others by role-taking and empathising.

Alternatively, the Central Coherence Theory (Happe, 1994a; Frith, 1989) is described by Frith (1989, p. 101) "as the tendency to process information holistically, and to derive balanced, integrated information through the competency of that

processing method". Central coherence "compels human beings to give priority to understanding meaning" (Frith, 1989, p. 101). On the other hand, weak central coherence results in the opposite tendency to process information in a piecemeal fashion, while paying a disproportionate amount of attention to unrelated detail. This results in a failure to see the whole picture and leads to the loss of overall meaning.

2.8.9.8 Executive Functioning and Autistic Spectrum Disorders

Executive Functions (EF) are thought to involve several interacting but dissociable mental processes, such as working memory, inhibition, mental flexibility and planning (Dennis, 1991). An alternative hypothesis to impairments in Theory of Mind being the core central deficit of autism is that of a deficit in Executive Function. Damasio and Maurer (1978) state that deficits in Executive Functioning can account for the rigid and repetitive behavioural patterns seen in autistic children, as well as impairments in communication and reciprocal interaction. Ozonoff, Pennington and Rogers, (1991a) have also proposed that performance on measures of Executive Functions are better indications of autism than is performance on ToM tasks. Effective social and communicative behaviours require on-line updating, evaluation, and the selection of appropriate responses, which are all areas of impairments in autistic children (Benetto, Pennington & Rogers, 1996).

Previous research on three to five year olds have found that performance on Executive Functioning tasks and Theory of Mind tasks are highly correlated. Perner and Lang (1999) conducted a meta-analysis and that found the relationship between Executive Functions and ToM was strong, but the correlation may be partly due to the similar demands of Executive Functions and ToM tasks put on the child, as both types of tasks require conflict and some form of inhibition of a response.

2.8.9.9 Section Summary

In summary, a consensus remains that Autistic Spectrum Disorders have a strong genetic component which alters brain development and results in behavioural impairment, in social and communication development, unusual narrow interests, and extreme repetitive behaviours. The biological basis of autism and the cognitive theories which have been suggested so far, demonstrate the heterogeneity in the aetiology of autism. This heterogeneity may account for the different manifestation often observed in the symptomatology of the disorder.

Nevertheless, most autistic children, share, to some degree, the three main areas of behavioural difficulties characterised by the "triad of impairment" (Wing & Gould, 1979), but their disorder will affect them in very different ways, depending on the co-morbidity with other conditions, associated intellectual disability, sensory impairments, and challenging behaviours that are often associated with Autistic Spectrum Disorders.

2.9 Chapter Summary and aims of the experimental components of the thesis

In summary, the two literature reviews have shown that the three clinical syndromes and autistic disorders are show similarities, as they both have had environmental or genetic factors implicated in their aetiology.

The experimental work in this thesis is arranged in four chapters. The experiments evolve from the findings of earlier Chapters, and so do the conceptual ideas and these will be discussed collectively in Chapter Seven.

It is anticipated, that the composition of the cohort would generate three different hypotheses about the source of autistic traits within this cohort of patients. Specifically,

are the origins of children's autistic behaviours in the present clinical cohort due to their hormonal deficiencies, visual loss or their neurological impairments?

To achieve this objective, the present theses necessitated selecting an appropriate method to measure, and identify, autistic behaviours in a wide range of children, including children with impaired visual function and/or intellectual disabilities. Furthermore, Chapter Three's literature also considers the parallels between blind children and autistic children. Specifically, whether blind children follow a different pathway in their autistic behaviours to that of sighted children, or whether autism and blindness occur commonly together, due to sharing associated neurological involvement and early medical complications (Andrews & Wyver, 2005). This review was aided in the selection of an assessment tool which was sensitive to children's visual loss. These selected would be used to identify and measure autistic behaviours in children with Septo-Optic Dysplasia and Optic Nerve Hypoplasia in comparison to children with isolated Hypopituitarism. Secondly, the thesis will also begin to address some of the associated autistic phenomenology covered in the literature review in children with Septo-Optic Dysplasia and Optic Nerve Hypoplasia in comparison to children with isolated Hypopituitarism.

CHAPTER THREE

THE SELECTION OF AN ASSESMENT TO USE FOR THE MEASURMENT AND INDENTIFCATION OF AUTISTIC SPECTRUM DISORDERS IN CHILDREN WITH VISUAL LOSS AND/OR INTELLECTUAL DISABILITY.

3.1 Background to Chapter Three

Previous research in Chapter Two, identified that Autistic Spectrum Disorders are a common occurrence in children with Septo Optic Dysplasia and Optic Nerve Hypoplasia (Bahar, Brody, McCann, Mendiola & Slott, 2003; Garcia-Filion *et al.,* 2008; Haddad & Eugster, 2005; Ek, Fernell & Jacobson, 2005; Parr, Shaffer, Salt, & Dale, 2008). Chapter Two also reported that children with Septo Optic Dysplasia and Optic Nerve Hypoplasia can often display varying degrees and combinations of visual impairment, and/or intellectual disabilities (Garcia-Filion *et al.,* 2008). Due to this co-morbidity of visual impairments and intellectual disability in these children, several theoretical and methodological issues needed to be addressed, prior to any initial systematic measurement of Autistic Spectrum Disorders within the present thesis.

3.2 Overview of Chapter Three

The aim of the present Chapter is to firstly identify possible sources and types of autistic like symptomatology in children with visual loss. It is important to consider how the origins of autistic like behaviours in blind children could be an antecedent of an alternative developmental path to that of sighted children and truly autistic in their origin. To address this, the literature review will focus on research into blind children's social and communicative behaviours. Relevant research will be selected using the DSM-IV-TR (APA, 2000) criterion for the diagnosis of Autistic Spectrum Disorders as described in the literature review of Chapter Two.

Secondly, the literature review will address the methodological concerns of measuring autistic disorders in children with varying symptomologies through a systematic review of instruments used for the assessment of Autistic Spectrum Disorders. The literature review will then aim to identify appropriate assessments to use within the present clinical of children. The factors which will be taken into consideration prior to selection are; their effectiveness in differentiating between autism, Autism Spectrum Disorders and intellectual disability, their psychometric properties, the age range with which they could be used upon, and the time taken for administration.

Thirdly, the empirical component of this Chapter will assess the feasibility of using the selected instrument from the literature review to assess autistic phenomenology in children with varying degrees of visual impairments and intellectual disability, if modifications are made to this instrument. It is anticipated, that through addressing the methodological and conceptual issues in this Chapter, autistic disorders can be systematically investigated in children with Septo Optic Dysplasia, Optic Nerve Hypoplasia and isolated Hypopituitarism in the latter Chapters of the thesis.

3.3 Introduction to Chapter Three literature review

It is well documented that intellectual disability and autism commonly co-occur, and that both of these disorders also share similar behavioural profiles (La Malfa, *et al.*, 2004). This overlap in symptomatology can make it difficult to identify the nature and origin of autistic behaviours in children with intellectual disability, and this often leads to diagnostic overshadowing by Clinicians. The already complex issue of overlapping symptomatology becomes more problematic when children also present with visual impairments.

Autistic typed behaviours in blind children are commonly referred to as "blindisms" and at time are considered a typical phenomenology of blindness and autistic in their origin per se (Gense & Gense, 1995). However, the developmental path of children with severe visual loss is yet to be systematically investigated, and this leads to uncertainties into what would be a "typical" developmental path for blind children, in comparison to an "atypical" course of development (Andrews & Wyvers, 2005; Dale, 2008).

3.4 Literature review of the development of the blind

According to Ornstein (1975) the eye is the central avenue of personal consciousness. Thus, if at least 90% of our information about our world originates through vision, a blind child's impairment in their social and communicative behaviours would be completely understandable and expected. Accordingly, the literature review will begin to consider how some of the autistic-like phenomenology in the blind could be explained by the limitations that blindness poses on these areas of development (Lowenfeld, 1973).

Blind children's impairments in social interaction

The early social and communicative behaviours of visually impaired children can often mirror those behaviours of sighted autistic children. Commonly, impairments during the emergence of play and other verbal and non-verbal behaviours are frequently observed during blind children's development (Gense & Gense, 2002). Children with visual loss can show less creativity, imagination, (Burlingham, 1965; Sandler, 1968; Wills, 1963) and reduced incidences of social play, when compared to their sighted

peers (Bishop, Hobson & Lee, 2005; Fraiberg, 1977; Hughes, Dote-Kwan & Dolendo, 1999; Preisler 1993; Skellenger & Hill, 1998; Warren, 1994).

Reduced incidences of social play, inevitably impact upon some crucial aspects of social interaction, which include fewer incidences of turn-taking behaviours with caregivers (Sandler & Wills 1965), reduced incidences of initiating, and taking part in social games (Preisler, 1991). In addition, children with visual loss can appear aloof because sighted children are not experienced in interacting with their blind peers and this can inadvertently result in diminished frequencies of social interaction (Preisler, 1993). Differences in the types of play behaviours have been observed by Troster and Brambring (1994), who reported, in a group blind children aged between forty-nine to seventy-two months of age, that they tended to explore objects more frequently, and they engaged in more noise making activities than their sighted peers.

The behaviour of blind children can also mimic that of sighted autistic children during the emergence of play. For instance, blind children exhibit less curiosity in their surroundings, and consequently they may prefer to play in isolation (Brambring & Troster, 1992). However, this observation in typically developing blind children can be interpreted differently to that usually observed in sighted autistic children. Vision promotes reaching behaviours to objects and people, and thus curiosity in a child's environment, and these behaviours are predominately motivated due to sight (Brambring & Troster, 1992).

Even so, the majority of blind children do acquire play behaviours such as symbolic and functional play, but sometimes their lack of vision hinders their ability to show these skills to others (Lewis, Norgate, Collis & Reynolds, 2000). The disparity reported so far, can be explained by the restraints that blindness imposes on the types of activities an individual can engage in. This brings into question whether the delay, which

is commonly observed in the play behaviours of the blind children, is a pseudo phenomenon due to a loss in the acquisition of information, or rather a true delay in the acquisition of play due to impairments in information processing (Brambring, 2008). In addition, traditional symbolic toys might not be symbolic for visually impaired children and may not be used in the same manner to that of sighted children (Brambring, 1998).

Other areas of delay reported in the blind have been during the emergence of joint attention abilities during infancy. Difficulties about the existence, permanence of objects, relationship objects have to an individual, and their environment undoubtedly disadvantage blind children in acquiring full knowledge about actions and events, as blind children do not spontaneously reach for or request an object by looking at it (Bigelow, 2003). Despite this, caregivers are able to establish joint attention via alternative routes, specifically through social contact such as touching and tickling that is accompanied by language (Urwin, 1983).

Blind children's Impairments in communication

Looking at non-verbal behaviours in the blind, Fraiberg (1977) reported differences between sighted and blind children's social smiling. Fraiberg (1977) reported that blind children did not use smiling as a way to elicit a response from others, but rather in response to the behaviours of others. Iverson and Goldin- Meadow (1997) also reported reduced frequency of gestures in the blind when compared to sighted children. Blind children's gestures were body centred and related to objects which were close to them in proximity. However, when blind children spoke, they gestured at the same rate, referenced objects in the same way and conveyed the same ideas, using the same range of gestures as the sighted group of children.

With reference to impairments in communication and, specifically, language, Moore and McConachie (1994) reported that the acquisition of expressive language in the blind and severely visually impaired children, with no associated disabilities was highly advanced, when compared to their comprehension abilities. However, differences were reported in use of pragmatics, the reduced frequency of verbal turn- taking, shorter sentence utterances, and the reduced ability to read and use body language. Parents were more likely to initiate conversations, ask more questions, and language was used primarily to request an action. Similarly, both blind and sighted autistic children showed difficulties in understanding the pragmatics of language (Fraiberg, 1977; Olymbios, 1999), impairments in initiating and shifting between topics (Gense & Gense, 2002) and a higher percentage of echolalia was reported (Perez-Periera & Conti-Ramsden, 1999).

3.5 The Assessment of Autistic Spectrum Disorders in children with severe and complete visual loss.

From the review of literature so far, it has emerged that blind children show delays and impairment in their social and communicative behaviours. It is not clear, however, whether these behaviours are due to an alternative developmental pathway in blind children or autistic phenomenology due to deep neurological impairments. It is possible that many blind children's impairments in their social and communicative behaviours are not a result of autistic phenomenology, but rather due to a reduced incidence of visual input about their social world, which undoubtedly would leave them at a developmental setback compared to their sighted peer (Dale & Sonsken, 2002). However, autism and blindness are not mutually exclusive disorders, just as autism and intellectual disability are not. This is issue warranted the use a diagnostic tool, which did not over report or under report autistic behaviours due to diagnostic overshadowing.

Thus, it was vital to find a tool that gave blind children the maximum opportunity to exhibit a full range of behaviours.

A review of instruments used for the assessment of Autistic Spectrum Disorders.

Research has demonstrated that Autistic Spectrum Disorders can be measured in children with visual loss, if adaptations or exclusions of specific scoring criteria are made to instruments. Some assessments which have been used in this manner so far, have been the Autism Behaviour Checklist (ABC; Krug, Arick, & Almond, 1978) by Goodman and Milne (1995), and the Childhood Autism Rating Scale (CARS; Schopler, Reichler & Renner, 1988) by researchers, Rogers and Newhart-Larson, (1989), Ek, Fernell, Jocobson and Gillberg, (1998) and Hobson, Lee and Brown, (1999).

All of these studies greatly varied in their methodology, but all reported autistic-like behaviours in children with severe visual loss which was commonly attributable to greater degrees of neurological impairments (Ek *et al.*, 1998; Rogers & Newhart-Larson., 1987) or children's inability to share experience about their world (Brown *et al*, 1999; Hobson *et al.*, 1999). More importantly, since these publications, new methods to measure autism have emerged, and are now more commonly used to screen, and diagnose Autistic Spectrum Disorders. For these reasons, the present thesis required a preliminary review of assessment tools used to measure autistic behaviours and these are summarised in table 3.1.

Table 3.1: Preliminary review of assessment tools used to measure for autistic behaviours in children and adults

Author & Year	**Measure**	**Age-Range**	**Appropriate population use**	**No of Questions**	**Format**	**Time taken (mins)**	**Reliability -Test-retest -Inter-rater -Internal consistency**	**Validity**	**Diff. Diagnosis Between (discriminative) ASD Vs Non ASD**
In-depth assessment contributing to diagnosis of autism									
Skuse *et al* (2004)	*3di*	3-16 years	ASD, non ASD, Autism, ID	266 items	Computer interview to caregiver by trained examiner	45-90	-94% ->0.9 -Unknown	Excellent concurrent validity (ADI Vs 3di) Mean [Kappa] = 0.74	Excellent (Sensitivity 1.0; specificity 0.97
Lord *et al* (1994)	*ADI-R*	MA: 18 months to adult-hood	ASD, non ASD and ID	93 items	Semi-structure interview to caregiver by trained examiner	90-120	-High at item levels. -75% ADOS- Vs ADI-R (Mazefsky & Oswald, 2006).	Pilowsky Yirmiya, Shulman & Dover (1998) CARS Vs ADI-R = 87.5 % agreement	good at discriminating between mild ID

Author & Year	**Measure**	**Age-Range**	**Appropriate population use**	**No of Questions**	**Format**	**Time taken (mins)**	**Reliability -Test-retest -Inter-rater -Internal consistency**	**Validity**	**Diff. Diagnosis Between (discriminative) ASD Vs Non ASD**
Lord *et al* (2000)	*ADOS-G*	MA above 18.	MA above 18 months. ASD, non ASD and ID	Four Modules	observation trained examiner	30-45	-Good, but adequate across individual items. -0.59-0.82	Concurrent validity with ADI-R Vs ADOS-G (Howlin & Karpf, 2004)	Can distinguish between autism and PDD-NOS Sensitivity 100%-86% Specificity 100%-68% 90% at discriminating between ASD Vs non ASD
Wing *et al* (2002)	*DISCO*	3 years onward	ASD, non ASD and ID	319 items	Semi-structured interview. Clinician only	180	- good - >.0.75 -strong	Disco cut - off significantly related to clinical diagnosis (Leekham *et al.*, 2002)	
Rutter *et al*, (1988)	*CARS*	2 $^{+}$ onward	ASD, non ASD and ID	15 item	Rating scale observation or interview by trained examiner	30-60	- good - >0.74 - Moderate – good (DiLalla & Roger, 1994)	Concurrent validity= 0.80 (clinician Vs. CARS)	100% between autism and ID (Teal & Weibe, 1980)

Author & Year	**Measure**	**Age-Range**	**Appropriate population use**	**No of Questions**	**Format**	**Time taken (mins)**	**Reliability -Test-retest -Inter-rater -Internal consistency**	**Validity**	**Diff. Diagnosis Between (discriminative) ASD Vs Non ASD**
Gilliam *et al.*, (1995)	*GARS*	3^{+} onward	ASD, non ASD and ID	42 items	Interview/ question completed by teacher or parent	20min	-Unknown - 0.88 - 0.96	GARS Vs ABC = 0.94,Good (Gilliam, 1995)	
Stone & Hogan (1993)	*PIA*	Under 6 years		118 items 11 dimension	Observation by trained examiner	30-45	Adequate Adequate	Concurrent validity achieved with CARS	6 out of the 11 dimensions distinguished ASD
Krajer (1997)	*PDD-MRS*	< 2 years	ASD, non ASD and specifically for ID		Interview	30-60	Good Unknown	PDD-MRS misdiagnosis of 9% of autistic cases compared to clinician	Good
Brief assessment contributing to diagnosis of autism in young infants									
DiLovore *et al* (1995)	*PLADOS*	<6 years	ASD, non ASD and mild ID		Structured observation	30	Good	-Unknown -Good (Stone *et al.*, 1999)	Good at discriminating between ASD and ID (Stone *et al.*, 1999)

Author & Year	**Measure**	**Age-Range**	**Appropriate population use**	**No of Questions**	**Format**	**Time taken (mins)**	**Reliability -Test-retest -Inter-rater -Internal consistency**	**Validity**	**Diff. Diagnosis Between (discriminative) ASD Vs Non ASD**
Robins *et al* (2001)	*M-CHAT*	Infants	ASD, Non ASD Mild ID only		Parent and caregiver	Brief	Unknown	Unknown	Good at discriminating between non- autism and autism
Adrein *et al* (1992)	*IBSE*	Infants	ASD, non ASD and ID	33 items	Parent and caregiver	Brief	Overall reliability high. Item reliability good for 31 out of 33 items	Unknown	Good at discriminating between ID, non ASD and ASD
Nylander & Gillberg (2001)	*ASD/ ASQ*	Adults only	Adults only	10 items	Question-aire	Brief	Good	Unknown	Unknown
Berument *et al* (1999)	*ASQ*	3 years +	ASD, non ASD and ID	40	Question-aire	Brief	Good Unknown Good	Good	Good discriminative validity

Autism Diagnostic Observation Schedule – Revised = ADOS – G, Autism Diagnostic Interview – Revised = ADI- R, Autism spectrum disorder = ASD, Autism Screening Questionnaire = ASQ, Autistic Spectrum Disorder in Adults Screening Questionnaire = ASDASQ, Childhood Autism Rating Scale = CARS, The Gilliam Autism Rating Scale = GARS, 3di= The Developmental, Dimensional and Diagnostic Interview, 3di, Infant Behavioural Summarised Evaluation = IBSE, ID = intellectual disability, The Diagnostic Interview for Social and Communication Disorders = DISCO, Modified Checklist for Autism in Toddlers (M-CHAT), Parent Interview for Autism = PIA, Pre-Linguistic Autism Diagnostic Observation Schedule = PLADOS, Social Communication questionnaire = SCQ, Scale for Pervasive Developmental Disorder in Mentally Retarded Persons = PDD-MRS, MA = Mental Age

Review of prospective assessments to use for Autistic Spectrum Disorders from table 3.1

Prior to the DSM-IV (APA, 1994) and ICD-10 (WHO, 1993) the best choice for the assessment of autism had been the Childhood Autism Rating Scale (CARS; Schopler, Reichler & Renner, 1988) due to its flexible use as a quick interview schedule or observational rating scale. The Childhood Autism Rating Scale consists of fifteen items which include: relationships with people, imitation, affect, visual responsiveness, verbal communication, activity level, intellectual functioning and auditory responsiveness.

However, the scoring criteria of the Childhood Autism Rating Scale incorporates language impairments, intellectual skills, and intellectual ability for diagnosis of Autistic Spectrum Disorders, and these are prevalent areas of impairments in children with intellectual disabilities, genetic disorders and sensory impairments, which are not indicative of autistic disorders. The scale is also based on the outdated DSM-III-R criteria has been shown in research to miss children diagnosed with PDD-NOS and over-identify children with intellectual disabilities as being autistic (Perry, Condillac, Freeman, Dunn-Geier, & Belair, 2005; Pilowsky, Yirmiya, Shulman, & Dover, 1998). For these reasons, DiLalla & Rogers (1992) suggest that the scale should be used as a screening instrument only. For the present thesis the removal of the item "visual responsiveness" would be necessary, and items concerning intellectual ability and sensory functions would need to be disregarded or interpreted with caution.

Also under consideration is the Autism Behaviour Checklist (ABC; Krug, Arick & Almond, 1980) which can be used on children with severe intellectual disabilities. However, when compared to the Childhood Autism Rating Scale, the Autism Behaviour Checklist only correctly identified 88 percent of the autistic subjects, whereas the Childhood Autism Rating Scale correctly identified 98 percent of the autistic subjects

(Eaves & Milner, 1993). Further, Volkmar *et al.,* (1988) suggests that the scale should be used to assess general behaviour difficulties as many items describe general impairments rather than impairments associated with Autistic Spectrum Disorders.

The rating tool, the Gilliam Autism Rating Scale (GARS; Gilliam, 1995) is a behavioural checklist with four sub-scales consisting of stereotyped behaviours, communication, social interaction, and developmental disturbances reported excellent psychometric properties in individuals with intellectual disabilities, physical impairments, speech difficulties and emotional disturbances. Although, recently, researchers Lecavallier (2005), Sikora, Hall, Mazefsky and Oswalt (2006), and South *et al.*, (2002), all reported that the Gilliam Autism Rating Scale was not as effective as other instruments in detecting autism. South *et al.*, (2005) did report that when the cut-off points were lowered, sensitivity levels increased to a more acceptable kappa value of 0.8.

Recent and more advanced diagnostic tools such as the 3Di (Skuse *et al.*, 2004) and the DISCO (Leekham, Libby, Wing, Gould & Taylor 2002; Wing Leekman, Libby, Gould & Larcombe, 2002) both have demonstrated good psychometric properties and would have been effective to use for the present thesis. However, these measures could not be used as both scales are intended to assist in diagnosis and can only be administered by qualified clinicians.

More appropriately, the Autism Diagnostic Interview-Revised (ADI-R; Lord, Rutter & LeCouter, 1994; Rutter *et al.*, 2003) and the Autism Diagnostic Observation Schedule (ADOS; Lord *et al., 2000*; Lord *et al., 2001*) which are considered to be 'gold standard' instruments to use for the assessment of Autistic Spectrum Disorders (Cohen, 2003; Constantino *et al.*, 2003). However, Rutter *et al.*, (2003), suggested that caution should be used in interpreting the results of the Autism Diagnostic Interview-Revised in

very young children, particularly those with mental ages below twenty four months. O'Brien *et al.*, (2001) further recommends that the Autism Diagnostic Interview-Revised is most valid for individuals with a mild intellectual disability, and thus not appropriate for the present sample of children.

In contrast, the Autism Diagnostic Observation Schedule (ADOS; Lord *et al.*, 2001) has been used on children with various clinical syndromes and intellectual abilities such as; William's syndrome (Klien-Tasman, Mervis, Lord and Phillipos, 2007), children with developmental delays (Gray, Tonge & Sweeny, 2007), Fragile X syndrome (Farzin *et al.*, 2007), specific language impairments (Conti-Ramsden, Simkin & Borring, 2006), Angelman's syndrome (Bonati *et el.*, 2007), Prader- Willi syndrome (Milner *et al.*, 2005) and Joubert syndrome (Ozonoff, Williams & Millner, 1999). As the Autism Diagnostic Observation Schedule separates scores for social reciprocity, communication, and repetitive behaviours to diagnose autism, or Autistic Spectrum Disorders, this reduces the risk of individuals being diagnosed with the disorder because of inflated scores for certain domain (Lord & Risi, 1998).

The psychometric properties of the Autism Diagnostic Observation Schedule in relation to clinical diagnoses of autism versus pervasive developmental disorders (PDD) and non-pervasive developmental disorders, reported a sensitivity of 1.00 and specificity of .79 for children ranging in age from 15 months to 10 years (Lord *et al.*, 2001). Bolte & Poutska (2007) have demonstrated good rates of inter-rater and re-test reliability, internal consistency of 90.4 and sensitivity of 48.1 in differentiating between autism and other Autistic Spectrum Disorders.

Although, Gray, Bruce, Tonge and Sweeney (2007) state that for children with low developmental ages caution in the interpretation of Autism Diagnostic Observation Schedule algorithms diagnostic cut-off is warranted, and that the Autism Diagnostic

Interview-Revised and Autism Diagnostic Observation Schedule are best used in conjunction for clinical assessment. However, Lord & Risi, (1998) have commented that most assessments for autism will lose some of their specificity properties when used in individuals with profound learning disabilities, very young children (<5yrs old), and high functioning adults.

To address problems of developmental delays and the diagnosis of autism, Tomanik, Pearson, Loveland, Lane and Bryant-Shaw (2007) reported that whilst the Autism Diagnostic Observation Schedule initially helped to identify 75% of participants correctly as autistic this improved to 84% when the Vineland Adaptive Behaviour Scales (VABS; Sparow *et al.*, 1984) measure for adaptive functioning was applied in the analyses. Lord & Risi (1998) also state that as the Autism Diagnostic Interview-Revised and Autism Diagnostic Observation Schedule both separate scores for the domains, the risk of an individual being diagnosed as autistic due to inflated scores for a certain domain is reduced.

Often, the screening tool, the Social Communication Questionnaire (SCQ; Berument, Rutter, Lord, Pickles, & Bailey, 1999) which is based on the Autism Diagnostic Interview – Revised is commonly in conjunction with the Autism Diagnostic Observation Schedule. The Social Communication Questionnaire has established good levels of validity, with good sensitivity at 0.85 and specificity at 0.75 in a sample of two hundred children (160 with Autistic Spectrum Disorders and forty children with language impairments and developmental delays), when the cutoff if ≥ 15 was used to differentiate between Autistic Spectrum Disorders and non-spectrum disorders (Berument, Rutter, Lord, Pickles, & Bailey, 1999). Berument *et al.*, (1999) reported mean scores for typically developing children of 5.2, mean scores for children with intellectual disabilities of 12.8, mean score for children with PDD of 22.3, and for children with autism

the mean score was 24.2. There was also a high correlation with the ADI-R algorithm scores ($0.71; p < 0.0005$).

Bishop and Norbury (2002) also found that the Social Communication Questionnaire was able to classify children with an Autistic Spectrum Disorders in children with speech and language impairments. Howlin and Karpf (2004) also used the Social Communication Questionnaire as a screening tool for individuals with Cohen syndrome and individuals who scored fifteen and above on the Social Communication Questionnaire were latee assessed using the Autism Diagnostic Observation Schedule and/or ADI-R. They reported that thirty out of the thirty-four individuals met the criteria on both diagnostic tools.

Summary of aims of Chapter Three

Taking into consideration these theoretical and methodological issues, the Autism Diagnostic Observation Schedule was selected for use in the present thesis as they both allowed certain items to be eliminated from the scoring process and both could be used on children with intellectual disability. However, it was considered that adaptations to the materials and scoring criterion of the Autism Diagnostic Observation Schedule would be required.

Therefore, the aims of chapter three are to:

- Assess whether modifications to the Autism Diagnostic Observation Schedule tasks and algorithms would elicit similar responses to that of the original Autism Diagnostic Observation Schedule tasks and algorithms.

- Assess the feasibility of using an adapted version of the Autism Diagnostic Observation Schedule in children with varying degrees of visual loss and intellectual disabilities in comparison to the original Autism Diagnostic Observation Schedule.
- Begin to consider whether the modified Autism Diagnostic Observation Schedule could be used to identify and measure autistic behaviours in children with Septo-Optic Dysplasia and Optic Nerve Hypoplasia in comparison to children with isolated Hypopituitarism in Chapter Four.

3.6 Methods

Participants

Thirteen children, with Autistic Spectrum Disorders, and a mild to moderate learning disability took part, of which, nine were boys and four were female. Children were aged between five years to fourteen years of age, and had a collective mean age of 8.4 years (SD = 1.6). Four children were echolalic, one child was preverbal, and for the remainder of children verbal expressive abilities were within the normal range. Ten typically developing children aged between three and eight years of age with a mean age of 5.4 years (SD = 1.2) were recruited. From the ten children, eight were male and two were female.

Eighteen children with varying degrees of visual impairments completed the modified and/or the standard Autism Diagnostic Observation Schedule; ten were female and eight males. The mean age of this group was 13.68 years (SD = 2.8; Range 5 to 16). Seven of these children were totally blind, three children demonstrated some light perception, two children had limited vision and six children had useful vision. Three children were unable to complete the assessment due to profound disability, two children

were too ill to take part and one child was off school for a prolonged period of time during the month of assessments.

Children were split into four groups according to their diagnosis, 1) Autistic Spectrum Disorders, 2) Typical development, 3) Moderate visual impairments and intellectual disability (functional vision) and 4) Blindness and intellectual disability (complete visual loss/light perception).

There were no inclusion or exclusion criteria, as the aim of the study was to assess the adaptations made to the Autism Diagnostic Observation Schedule materials on a wide range of children with visual impairments. Table 3.2 shows the individual sample characteristics of each child and table 3.3 shows the group sample characteristic of all children. Criteria for the level of visual function, and intellectual ability were provided to the researcher by the head teacher of the school prior to the study commencing.

Table 3.2: Child sample characteristic of children with visual impairments

Child no	Sight	Module	Age	Gender	Verbal level	Physical disability	*Ability level
1.	LP	1	10	Female	Pre-verbal	Yes – mobility help	profound
2.	LP	1	12	Female	Preverbal	Wheel chair user and hearing aid	profound
3.	LP	1	13	Female	Pre-verbal	Yes – mobility help	profound
4.	LV	1	8	Male	Pre-verbal	Wheel chair user	profound
5.	LV	1	12	Female	Pre-verbal	Yes – mobility help	profound
6.	TB	1	14	Female	pre-verbal (non verbal)	No	moderate to severe
7.	TB	1	8	Male	Pre-verbal	Yes – mobility help and a hearing problem	profound
8.	TB	1	11	Male	Pre-verbal	Yes – mobility help	profound
9.	TB	1	12	Male	Pre-verbal	Yes – mobility help	profound
10.	TB	1	9	Female	pre-verbal	Yes – mobility help	profound
11.	UV	1	9	Male	phrase speech (echolalic)	Yes – mobility help	profound
12.	UV	1	11	Female	Phrase speech	Yes – mobility help	profound
13.	UV	1	14	Male	Phrase speech	Yes – mobility help	profound
14.	UV	1	15	Female	Pre-verbal	Yes – mobility help	profound
15.	UP	2	14	Female	Fluent speech	No	moderate
16.	TB	4	13	Male	Fluent speech	No	moderate
17.	TB	4	17	Male	Fluent speech	No	moderate
18.	UV	4	16	Male	Fluent speech	No	moderate

Table 3.3: group sample characteristic of children with visual loss

ADOS Modules	One	Two	Four
N	14	1	3
Gender	F= 8,M= 6	F=1	M=3
Visual Acuity	5 TB, 3 = LP, 2=LV, 4 = UV	UV	2 TB
Verbal ability	13 pre-verbal	Verbal	Verbal
Age Range and Mean	12.7 (SD = 2.8 Range 5-16)	12.4	16.2 (SD =0.2, Range 15-16.9)
Intellectual Ability	Severe- Profound	Moderate	Moderate
Physical Disability	60%	None	None

**Useful vision = UV, Totally Blind = TB, Limited Vision = LV, Light Perception*

Recruitment

Four schools, which specialise in teaching children with Autistic Spectrum Disorders and/or intellectual disabilities were approached in the Birmingham area, with an invitation pack about the project, a sample parent invitation sheet and consent form (Appendix A). One school accepted the invitation to take part in the pilot study. Fifty invitation packs (Appendix A) were sent to parents on the behalf of the researcher by the deputy head of the school. Typically developing children, from the same neighbourhood as the special school, were also recruited by the researcher.

Schools for the visually impaired within the Midlands, London and Liverpool were identified through the Royal Society for the Blind website. All schools were contacted with an invitation sheet (Appendix B) and acknowledgement sheet (Appendix B). Included was an invitation, information sheet for parents (Appendix B) and a parental assent form (Appendix B) for parents. One school accepted to take part in the study and thirty students were selected by the deputy head to take part in the study, as

they were considered to be a representative sample population of the school. Twenty four consent forms were returned to the school by parents.

Measures and Procedure

The Autism Diagnostic Observation Schedule

The Autism Diagnostic Observation Schedule is a semi-structured standardised assessment of communication, social interaction and play or imaginative use of materials. By making use of "planned social occasions" the Autism Diagnostic Observation Schedule facilitates observation of the social, communication, and play or imaginative use of material behaviours related to the diagnosis of ASD. Previous research has identified that impairments in these behavioural domains are crucial indicators of suspected autistic tendencies in children (Lord *et al*, 1998). The schedule also examines speech abnormalities, stereotyped and restricted interests. However, the Autism Diagnostic Observation Schedule does not utilize impairments in these areas for diagnosis of autism mainly due to these behaviours frequently occurring in children with learning disabilities and/or visual impairments

The Autism Diagnostic Observation Schedule consists of four modules, each of which is appropriate for individuals who differ in developmental ability and language acquisition, ranging from no expressive language to some receptive language to verbally fluent. Module one is designed for individuals who are preverbal or who speak in single words, Module two for those who speak in phrases, Module three for children and adolescents with fluent speech, and Module four for adolescents and adults with fluent speech. Administration of the Autism Diagnostic Observation Schedule requires 30 to 45 minutes and provides social-communication sequences that involve "presses" for particular social behaviours.

The Autism Diagnostic Observation Schedule was modified to take into account children's visual impairments. Toys which relied heavily on visual stimulation were substituted for toys that are more tactile and auditory in nature. The adaptations made to the materials aimed still to measure/elicit the same behaviours as the original Autism Diagnostic Observation Schedule toys (see Appendix C for the changes to instructions and materials). A catalogue produced by the Royal National Institute of the Blind (RNIB) provided a selection of toys suitable for blind and partially sighted children for substitutions. Table 3.4 summarises the adaptations made to the Autism Diagnostic Observation Schedule.

Table 3.4: Changes to Autism Diagnostic Observation Schedule modules tasks

TASKS	CHANGES
Module 1. Expressive language level – no speech/ simple phrase	
1.Free play	No change, tactile exploration of items is encouraged
2.Response to name	No change
3. Response to joint attention: Purpose: elicit eye contact coordination with facial orientation, verbalisation, and pointing in order to draw the child's attention to a distant object	The child's name is called or the child is touched to attract their attention and the examiner says "look/what's that noise". The examiner waits to see if the child requests the toy by reaching, looking, and/or vocalising.
4. Bubble Play	Directed to part of body (arm)
5. Anticipation of a routine with objects	No change except, blind child's hand is place on examiner
6. Responsive social smile	No change
7. Anticipation of a social routine	No change
8. Functional and symbolic function.	Child's hand is placed on top of examiner's hand
9. Birthday party	No change - tactile exploration of items is encouraged
10. Snack	No change
Module 2: Expressive language level – flexible three word phrases/ verbally fluent	

1. Construction task:	Tactile matching puzzle completion task from RNIB.
2. Response to name	No change
3. Make -believe play	No change - tactile exploration of items is encouraged
4. Joint interactive play	No change - tactile exploration of items is encouraged if appropriate
5. Conversation	No change
6. Response to joint attention	No change - tactile exploration of items is encourages
7. Demonstration task	No change, except, blind child's hand is place on examiner
8. Description of picture scene	An appropriate language sample has been generated during book telling or conversation.
9. Telling a story from a book.	A braille book chosen from articles for the blind
10. Free play	No change, tactile exploration of items is encourages
11. Birthday party	No change - tactile exploration of items is encourages
12. Snack	No change
13. Anticipation of a routine with object	No change - tactile exploration of items is encourages
15 Bubble play	Directed to part of body (arm)
Module 3-Expressive language level – verbally fluent/ child to adolescent.	
1. Construction task:	As module two
2. Make -believe play	No change, tactile exploration of items is encouraged
3. Joint interactive play	No change, tactile exploration of items is encouraged
4. Demonstration task	No change, except, blind child's hand is placed on examiner to guide over objects or to set the scene
5. Description of a picture	As module two
6. Telling story from book	As module two
7. Cartoons	No change, pictures verbally described
8. Conversation and reporting	No change
9. Emotions	No change
10. Social difficulties and annoyance	No change
11. Break	No change
12. Friends and marriage	No change

13. Loneliness	No change
14 Creating a story	No change, tactile exploration encourages and items are described
Module 4 -Fluent speech/child/Adolescent	
1 4-13, 15 as module three	As module three
11.Daily living	No change
5. Current work and school	No change
15.Plans and hopes	No change

Procedure

All children completed the modified parts of Autism Diagnostic Observation Schedule, which was tailored for children with severe visual impairments. The original corresponding task of the Autism Diagnostic Observation Schedule was completed a week later for all children with functional vision. Blind children and children with only light perception completed the full Autism Diagnostic Observation Schedule but with the modified Autism Diagnostic Observation Schedule materials which took into account their visual loss

Prior to administration the head teacher of the school provided information about each child's visual function, verbal ability and age. All Autism Diagnostic Observation Schedules were coded in a quiet room with a teaching assistant present. Video recordings were not taken of the assessments on the request of the school and all of the eighteen assessments were completed in a four week period. The Autism Diagnostic Observation Schedule was scored immediately after each live administration and item ratings were copied into the algorithm form provided for each subject.

Thresholds for autism and for Autistic Spectrum Disorders were applied to each of the domain scores and the total score. Appendix D identifies the algorithm items

which relied heavily on vision and the adaptations which were made to make allowances for children who are visually impaired.

Data analysis strategy

Exploratory analyses were initially conducted to establish whether data met parametric assumptions. Shapiro–Wilks W tests revealed no significant statistically differences on the raw algorithm scores of the Autism Diagnostic Observation, which lead to the assumption that the distribution was normal. Although, non-parametric tests were used when group sizes were considerably unequal or small.

Firstly, *t*-tests were used to assess differences between the original and modified Autism Diagnostic Observation Schedule between children with autistic phenomenology and typically developing children. As the reliability and validity of the Autism Diagnostic Observation Schedule had been investigated in these two groups of children in prior research (Lord *et al.*, 2000), children with moderate visual impairments were excluded from this first analysis. Secondly, children with Autistic Spectrum Disorders, typical development and limited vision were compared on the adapted and original corresponding tasks on the Autism Diagnostic Observation Schedule, using a two by three ANOVA. All four groups of children were then compared on the modified tasks of the Autism Diagnostic Observation Schedule. Lastly, the performance of children with complete visual loss and visual impairments was investigated, as this group of children completed the full Autism Diagnostic Observation Schedule.

3.7 Results

Table 3.5 shows the mean and *t*-tests which revealed no significant differences between the original and modified Autism Diagnostic Observation Schedule, thus demonstrating that performance was similar on the modified and original version of the Autism Diagnostic Observation Schedule in children with autism and/or intellectual disability and typically developing children.

Table 3.5: The modified and original version of the ADOS means score and statistical analysis of children with autism and/or intellectual disability and typically developing children

ADOS task	Original task	Modified task	*t*	*df*	*p-value*
Construction task					
Requesting	.36	.30	1.00	32	.32
Vocalisation	.30	.32	.00	32	1.0
Gesture	.48	.42	1.0	32	.33
Eye contact	.52	.55	.33	32	.74
Joint attention					
Pointing	.45	.51	.70	32	.49
Telling a story from a book					
Overall level of non-echoed language	.39	.51	1.23	32	.21
Amount of social overtures/maintenance of attention	.36	.24	2.10	32	.11
Speech abnormalities with autism	.51	.61	.90	32	.37
Immediate echolalia	.48	.54	.63	32	.56
Empathy (module three and four)	.61	.69	.90	32	.37
Bubble play					
Affect	.40	.58	1.28	32	.21
Shared enjoyment	.33	.42	1.14	32	.26
Requesting	.27	.36	21.14	32	.26
Initiation of joint attention	.39	.48	1.36	31	.18

Comparison of raw algorithm scores between children with typical developmental, Visual Impairments and Autistic Spectrum Disorders

A two (modified Vs original) by three (child condition) mixed-model ANOVA revealed that a main effect for Autism Diagnostic Observation Schedule presentation was not statistically significant; $F(2, 28) = 4.70$, $p > .01$, Eta-squared = .25, however at a less conservative significance level of 0.05, statistically significant differences were achieved between children with autism, typical development and visual impairments ($F(2, 28) = 4.70$, $p < .05$, Eta-squared = .25) but using a conservative 0.01 significant level, there was no overall difference between the algorithm task scores of the standardised task (M = 5.81) compared to modified task (M = 5.80) for all children. No significant main effect for condition status was obtained, $F(2, 28) = .12$, $p < .01$, though this was a weak effect (Eta-squared = .04).

Furthermore, no significant differences between task presentation and child condition status was obtained, $F(1, 28) = 1.53$, $p > .01$, and this was a weak effect (Eta-squared = .10). Examination of the cell means indicated no large increase in Autism Diagnostic Observation Schedule scores for children with autism from the standardised task (M = 10.00) to modified task (M = 10.17), children with typical development from the standardised task (M = 0.00) to modified task (M = 0.00), and children with visual impairments from the standardised task (M = 6.25) to modified task (M = 6.13).

Comparison of children with visual impairment and intellectual disability

There were statistically significant differences between children with ASD, Typical Development, Visual Impairments and complete Blindness, on the modified Autism Diagnostic Observation Schedule. Looking at the mean rank scores in table 3.6, children with ASD and blindness performed similarly, compared to children with typical

development or children with visual impairments on the modified Autism Diagnostic Observation Schedule.

Table 3.6: Comparison between children with visual impairment, blindness, typical development on the mean rank score and statistical analysis of total raw ADOS algorithm for modified tasks only

ADOS modified	N	Mean Rank	X^2	N	*p-value*
ASD	13	26.12	12.32	3	0.01
Typical Development	10	11.00			
Visual Impairment	8	20.00			
Blind	10	25.15			

Comparison of children with visual impairment and intellectual disability

In total, 55% of participants scored above the cut-off point, with four individuals satisfying the Autistic Spectrum Disorders cut-off point, and four children scored above the cut-off point for autism. After adjustment of scores according to the child characteristics outlined in table 4.1, individuals with severe to profound intellectual disability were removed. Even after the removal of profound intellectual disability, 44% of children still reached the cut-off points for Autistic Spectrum Disorders, with five children meeting the cut-off point for Autistic Spectrum Disorders and three children satisfied the criteria for autism. The mean scores on each of the domains of the adjusted Autism Diagnostic Observation Schedule are shown in figure six.

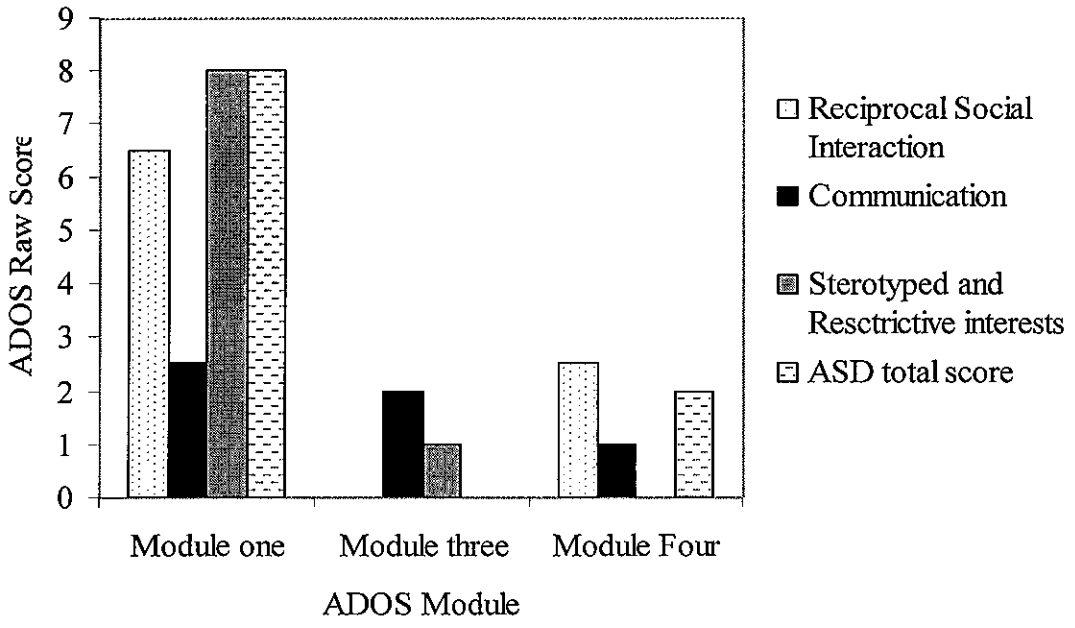


Figure six: the mean scores on each of the domains of the adjusted ADOS

Figure Six, shows that all cases of autism and Autism Spectrum Disorder occurred in module one, a group which had the highest degree of visual loss, intellectual disability and physical disability. The visual acuity of children who met the cut-off points for autism/ASD was varied with; three children totally blind, two with light perception, one had limited vision and two children demonstrated useful vision.

The Autism Diagnostic Observation Schedule algorithm sheet allows the examiner to make notes on the behaviours observed in order to score items appropriately. During the study "stilling" was observed to indicate attention to a task, orientating of children's bodies or heads around to the source of a sound were observed during the "response to joint attention" and "bubble play" tasks of module one.

Reaching in proximity to the source of auditory materials, either to request or point was recorded on several occasions. It was difficult to differentiate between pointing and requesting, however, requesting an object included increases in vocalisations and arm movements. Arm movements occurred in higher intensity and

more indiscriminately and usually diminished once the target object was in grasp. No pointing was observed in any children from a distal point as most objects were explored tactilely.

Possible joint attention was achieved during activities which included touch of bubbles blown on a child's arm and reaching in the direction of the toy with vocalisations. In two instances blind children orientated their head to the examiner at the point at which the examiner said "what's that", once the bubble popped on the children's arm. Upper body orientation, increase in rocking head towards the ceiling and table and touching of the area where the bubble popped was also observed. One child got up to search for the source of the bubbles and pulled on the examiner to request more bubbles. Vocalisations which were not always directed to the examiner, increased when the child was touched and/spoken too. Adaptations for bubble play showed that children would still request by vocalisation or reach towards the bubble gun accompanied by social smiles.

3.7 Discussion

The current study is the first to have assessed the feasibility of using the Autism Diagnostic Observation Schedule in children with intellectual disability and visual impairments. The aims of the present study were to firstly assess whether modifications to the Autism Diagnostic Observation Schedule tasks and algorithms would elicit similar responses to that of the original Autism Diagnostic Observation Schedule tasks and algorithms. Secondly, the study aimed to assess the feasibility of using an adapted version of the Autism Diagnostic Observation Schedule in children with varying degrees of visual loss and intellectual disabilities in comparison to the original Autism Diagnostic Observation Schedule. Lastly, based upon the data found, the study began to

consider whether the modified Autism Diagnostic Observation Schedule could be used to identify and measure autistic behaviours in children with Septo-Optic Dysplasia and Optic Nerve Hypoplasia in comparison to children with isolated Hypopituitarism (See Chapter Four).

The present study reported that the original Autism Diagnostic Observation Schedule can be used for children who display both moderate to severe levels of intellectual disability and mild to severe levels of visual impairments. Furthermore, the modified Autism Diagnostic Observation Schedule should be used for children with complete visual loss or profound visual loss (e.g., light perception only).

Comparison between the Modified Autism Diagnostic Observation Schedule and the original Autism Diagnostic Observation Schedule.

When typically developing children, children with autistic disorders and children with intellectual disability were compared collectively on the raw scores of the original and modified Autism Diagnostic Observation Schedule no statistically significant differences were reported. This showed that, regardless of symptomology, the modified and original Autism Diagnostic Observation Schedule elicited similar responses, and that the changes to the Autism Diagnostic Observation Schedule did not alter how children performed on both versions of the Autism Diagnostic Observation Schedule.

Secondly, when visually impaired children with severe intellectual disability were compared on the standard and modified modules of the Autism Diagnostic Observation Schedule similar responses were elicited on both versions. However, elevated algorithm scores on the Autism Diagnostic Observation Schedule were reported when children presented visual impairments, physical disability and/or intellectual disability.

Furthermore, statistically significant differences were found between children with Autistic Spectrum Disorder, typical development, visual impairments and complete visual loss, on the modified Autism Diagnostic Observation Schedule. Children with Autistic Spectrum Disorder and blindness performed similarly, compared to children with typical development or children with visual impairments on the modified Autism Diagnostic Observation Schedule. When interpreting this finding, it is important to consider that children were not matched between groups on their levels of intellectual disability and children with visual loss demonstrated greater degrees of intellectual disability. Knowing that children with severe levels of intellectual disability are more vulnerable to autistic phenomenology it becomes increasingly difficult to decide whether the elevated scores in children with visual impairments were an antecedent of their severe to profound levels of intellectual disability, or of their visual loss.

The feasibility of using an adapted version of the Autism Diagnostic Observation Schedule in children with varying degrees of visual loss and intellectual disabilities

The flexibility of using the original and adapted Autism Diagnostic Observation Schedule in such a heterogeneous group of children was demonstrated because the majority of children could complete the assessments. Even so, children who demonstrate low developmental ages Autism Diagnostic Observation Schedule algorithms diagnostic cut-off is scores should be interpreted with caution (Gray, Bruce, Tonge & Sweeney' 2007). Furthermore, they state that the ADI-R and Autism Diagnostic Observation Schedule are best used in conjunction, for clinical assessments.

However, Lord and Risi, (1998) have commented that most assessments for autism will lose some of their specificity properties when used in individuals with profound learning disabilities, very young children (<5yrs old), and high functioning

adults. All children who completed module one had severe intellectual disability and were generally older than expected.

Looking at children's responses in detail "pointing", elevated the scores in the communication domain. The study demonstrated that, as pointing is usually directed towards an object which can be seen rather than heard, blind children usually vocalised for requesting rather than pointing. Fraiberg (1997) also observed the reduced incidence of blind children pointing, and as pointing helps to gain the attention of others, this has been proposed as an explanation in the reported delays observed in blind children acquiring joint attention skills which could have elevated scores in the present study in children with a visual impairment.

Even when unusual eye contact was eliminated from the coding of domain "reciprocal social interaction", elevated scores were still observed due to facial expression, showing that initiation and response to joint attention all elevated scores considerably in children with functional vision.

The adaptation to "response to joint attention" saw some children "stilling" to sounds and turning of their bodies. The research study therefore supports the idea that establishment of joint attention via an alternate route, specifically through social contact such as touching and tickling accompanied by language. In support, the study confirms the importance's of shared references which are often restricted to verbal exchanges within visually impaired children (Mulford, 1983).

Frequently observable delays in symbolic play are exhibited in children who are blind. Once again, this delay may be explained by two different factors. Firstly, traditional symbolic toys, like dolls or cars may not be interesting for blind children, because they are more visually represented, and hence do not correspond tactilely or by sound, to the real objects that they represent (Troester & Brambring, 1994). Secondly,

investigators may be unaware of the alternative forms of symbolic play in children who are blind, such as verbal role play (Ferguson & Buultjens, 1995), and as a result, they may miss blind-specific forms of symbolic play.

With the lack of previous research into alternative forms of joint attention abilities and forms of pointing in the blind, and the small sample size for the present study, The algorithm scoring for these activities on the modified Autism Diagnostic Observation Schedule was always scored as zero for children with profound visual loss.

Consideration for the utilisation of the modified Autism Diagnostic Observation Schedule for the present clinical cohort.

The final aim of the research study was to consider whether the modified Autism Diagnostic Observation Schedule could be used to identify and measure autistic behaviours in children with Septo-Optic Dysplasia and Optic Nerve Hypoplasia in comparison to children with isolated Hypopituitarism (See Chapter Four). It was considered that the modified Autism Diagnostic Observation Schedule was successful in eliciting similar responses in children to that of the original Autism Diagnostic Observation Schedule. It was highlighted that the validity and reliability of Autism Diagnostic Observation Schedule needed to be considered. It is anticipated, that through the utilisation of other measures which are used to assess for autistic disorders, and statistical analysis of the psychometric properties of these measures, this can be achieved. This will be initially addressed in the empirical component of Chapter Four, prior to the systematic investigation of autistic phenomenology in children with Optic Nerve Hypoplasia, Septo Optic Dysplasia and isolated Hypopituitarism.

Limitations and future suggestions

The limitation of the present study was the small sample size, lack of young children and the high degree of intellectual disability. Most importantly, children with varying degrees of visual impairments needed to be matched to autistic children, according to their intellectual ability, age, and gender, but due to difficulties in recruitment, this was not achieved. Children with visual impairments and no associated intellectual impairments more frequently attend mainstream schools, however this group proved to be difficult to access. Future research would need to examine how joint attention abilities, pointing, gestures and showing are achieved in a large sample of blind children with and without intellectual disability and whether impairments in these areas result in elevated scores on the Autism Diagnostic Observation Schedule. Furthermore, if the developmental path of these behaviours can be mapped in the congenitally blind children and applied to area of autism and visual impairments this may help to answer questions about the sources of similarities between the two conditions.

Chapter Summary

In conclusion, the present study reported that the modified Autism Diagnostic Observation Schedule could be used on children with varying degrees of learning disabilities and visual impairments. When used on children with severe to profound intellectual disability and visual impairments scores need to be interpreted with caution due to overlapping behavioural characterises in these two disorders.

Most importantly, the study highlights the lack of research into the development of a standardised assessment to assess autistic phenomenology in children who display varying levels of intellectual and sensory disabilities. The lack of appropriate diagnostic tools can lead to diagnostic overshadowing, which can ultimately leave children without

the appropriate medical and educational provisions. Reasons for an absence of such a tool, appear to be due to an uncertainty into what is a "typical" development path for a blind child, and that most current assessments rely heavily on impairments in joint attention abilities and eye gaze alterations in their diagnostic criteria. Furthermore, when diagnostic assessments are altered this reduces their psychometric properties.

Inadvertently, the study also highlights that the "gold standard" assessments need to be inclusive of all children's disabilities, and this lack of inclusive assessment instruments for autistic disorders leave many children overlooked for the diagnosis of autism.

CHAPTER FOUR

THE IDENTIFICATION AND MEASUREMENT OF AUTSITIC SPECTRUM DISORDERS IN CHILDREN WITH SEPTO OPTIC DYSPLASIA, OPTIC NERVE HYPOPLASIA AND ISOLATED HYPOPITUITARISM.

4.1 Background to Chapter Four

The literature review in Chapter Three reported that a number of assessments can be used to identify Autistic Spectrum Disorders in children with varying degrees of intellectual disability, but differences began to emerge between these assessments when their psychometric properties and ease of application were taken into consideration. The systematic review of Chapter Three also identified that researchers and Clinicians were increasingly advocating the use of the Autism Diagnostic Observation Schedule for the diagnosis of autism, due to the schedule's robust psychometric properties and ease of application for children with varying degrees of developmental disabilities (Lord & Risi, 1998).

Notably, Chapter Three reported that current screening tools and diagnostic instruments did not allow for the testing of autism in children with visual impairments and/or intellectual disability, even though autism was known to be a common occurrence in numerous ophthalmologic conditions (Chase, 1972; Chess, Corn & Fernandez, 1971; Fazzi, *et al.*, 2007; Fraiberg, 1977; Gense & Gense, 2005; Hobson *et al.*, 1999; Hobson & Bishop 2003; Keeler, 1958). In order to identify autistic symptomology, previous research adapted or excluded diagnostic criteria and/or methods, but with the advent of more rigorous methods to assess autism much of this

research is now outdated. Furthermore, no consideration had been given to the psychometric properties of these instruments.

Based on previous research and the availability of more appropriate measures to assess autistic phenomenology, Chapter Three selected the Autism Diagnostic Observation Schedule. Adaptations were made to the materials, procedure, and scoring criteria and these took into account children's visual impairments. The adaptations to the schedule were found to be an effective measure of autistic behaviours in a group of children with varying degrees of visual loss and intellectual disability, and the adapted schedule was selected to use on the current cohort of children for this Chapter.

4.2 Overview of Chapter Four

To address the phenomenon of autistic disorders in children with visual impairments, Chapter Four will review literature that examines the theoretical explanations for the heightened occurrence of autism in children with visual loss. The review will also explore reported prevalence rates of autism in groups of children with homogenous ophthalmologic conditions and large scale group studies of heterogeneous ophthalmologic condition. It is anticipated that the literature review will support the requirement for the creation of an appropriate measure to diagnose autism in children with visual loss and offer theoretical explanations for the heightened occurrence of autism in children with Septo-Optic Dysplasia and Optic Nerve Hypoplasia.

The empirical component of Chapter Four will aim to assess initially the psychometric properties of the Autism Diagnostic Observation schedule, as research has yet to explore this. The psychometric properties of the schedule will be assessed in

comparison to the Social Communication Questionnaire, the Gilliam Autism Rating Scale, and Clinician diagnosis for children with Septo Optic Dysplasia, Optic Nerve Hypoplasia and isolated Hypopituitarism. The Social Communication Questionnaire was selected as previous research indicated that this screening questionnaire was commonly used with the Autism Diagnostic Observation Schedule for the assessment of autism. Secondly, the Gilliam Autism Rating Scale was selected due to its ease of application and for assessing the psychometric properties of the Autism Diagnostic Observation Schedule. Clinician diagnosis was also used in order to consider the validity of the Autism Diagnostic Observation Schedule.

The second aim of the empirical component of Chapter Four was to establish the prevalence rate of Autistic Spectrum Disorders in the present cohort of children. As this is the first study to systematically assess autistic disorders in the present population of children with Septo-Optic Dysplasia, Optic Nerve Hypoplasia and Isolated Hypopituitarism, this should begin to shed light on current prevalence rates of autism within these disorders across the United Kingdom. Whilst the establishment of higher rates of Autistic Spectrum Disorders has been reported in children with Septo-Optic Dysplasia and Optic Nerve Hypoplasia, the limitations of previous research is its use of small cohorts of patients, or of retrospective patient records, and the present Chapter aims to address these issues (Bahar *et al.*, 2003; Ek *et al.*, 2005; Parr *et al.*, 2008; Pring & Ockelford, 2005).

4.3 Introduction to Chapter Four literature review.

In 1958, Keeler initially documented the striking similarities between blind children, and sighted autistic children. Later in 1977, Fraiberg in her seminal book "insights from the blind" reported on the behavioural profiles of twenty-seven cases studies of blind children. Interestingly, seven of the twenty-seven blind children exhibited the clinical profile of autism, and from these observations Fraiberg (1977) coined the term "ego deviation". What was striking was that nearly all of the twenty-seven children in her study showed some degree of motor stereotypy and peculiar mannerisms. However, the seven blind and autistic children also demonstrated stereotyped hand movements, body rocking, echolalia, unresponsiveness to others and, aloofness. In addition, all twenty-seven children encountered later developmental setbacks in learning Braille, developing attachments, and mastering language of "the self".

More recently, Gense and Gense (2005, p. 3-4) reported that the behaviours of some blind children, were "markedly difficult to generalise," when compared to "typically" developing blind children. For example, a number of children exhibited difficulties in developing language for the purpose of communication, and the language which they did acquire was mainly echolalic, limited in meaning, and their accompanying verbal speech was often flat in tone. After some time, children also encountered subsequent behavioural problems, specifically when relating to their peers, which often lead to withdrawal from social situations.

When Gense and Gense (2005) observed typically developing blind children, they found that their behaviours often mirrored the behaviours of sighted children with

Autistic Spectrum Disorders. Similarities included; perimeter hugging, stereotypy, echolalia, self absorption, and the need to touch everything. Nonetheless, they concluded that these behaviours served functional purposes for the visually impaired, and were not maladaptive behaviours per se, and were somewhat common to observe. For instance, the spinning of objects and body rocking were often seen as a process of sensory stimulation, due to the lack of visual stimuli, and not as a consequence of any autistic phenomenology. These autistic behavioural similarities in the blind are often referred to as; "blindisms", "autistic–like", or "autistic-tendencies", and usually diminish with appropriate behavioural interventions, and age (Hobson & Bishop, 2003; Hobson, Lee & Brown, 1999).

4.4 Literature Review on autism and blindness

Historically, behaviours exhibited by blind children were considered autistic-like and were attributed to a child's visual loss. Increasingly, clinicians and researchers have acknowledged that blindness and visual loss are not mutually exclusive disorders and can co-occur together.

Theoretical considerations of linking autism and blindness together

To date, researchers remain split on the nature and origin of autistic behaviours in children with visual impairments. On one side, "phenocopy" theorists suggest that blindness has certain developmental consequences, which include autistic-like behaviours such as echolalia, pronominal reversal, and the delayed emergence of pretend play (Fraiberg, 1977). Indeed Baron-Cohen (2002) suggests that autistic

behaviours observed in visually impaired children are only a surface similarity and not truly autistic in their origin. Therefore, such phenocopy features are transient and can improve with the appropriate behavioural interventions (Baron- Cohen, 2002).

Alternatively, "co-morbidity" theorists suggest, that blindness and autism occur more commonly together than predicted by chance, because they share common genetic and environmental antecedents (Chase, 1972, Chess, Fernandez & Corn, 1971; Keeler, 1958; Rogers & Newhart-Larson, 1989).

Intellectual disability, autism and blindness

Neurological damage to the brain underpins Autistic Spectrum Disorders and some eye conditions, such as Septo-Optic Dysplasia and Optic-Nerve Hypoplasia. This damage often results in intellectual disability, which is highly associated with Pervasive Developmental Disorders (Garcia-Filion *et al.*, 2008; Wing & Gould, 1979). For example, the Wing and Gould (1979) population study in London, noted that 56% of cases of Autistic Spectrum Disorders were associated with an intellectual disability. For the visually impaired, Garcia-Filion *et al.*, (2008), reported that 73% of children with Septo-Optic Dysplasia/Optic-Nerve Hypoplasia experienced developmental delays, and Rogers (1996) reported that 56% of visually impaired children in Liverpool, also had some form of an intellectual disability.

These findings raise the following questions when one considers autism in visually impaired children:

- Is autism induced by blindness, or coincidental neurological damage (Chase, 1972)?

- Are the behaviours of blind children attributable to visual impairments (Baron-Cohen, 2002)?
- Does a lack of vision, predispose children to autism or autistic- like features (Perez-Pereira & Conti-Ramsden, 1999)?
- Do some eye conditions predispose a child to autism more than others (Jordon, 1996)?

The environment, blindness and autism

Lowenfeld (1981) postulated that some of the autistic-like phenomenology in the blind could be explained by the limitations that blindness poses in three primary areas of development. Firstly, a reduced range, and variety of experiences limits the blind child. Secondly, the reduced ability to move around, and manipulate the environment, hinders the blind child's physical exploration of their social environment, and lastly, a lack of understanding about the "self" in relation to one's environment, may set in motion impairments in a child's social development.

To support the Lowenfeld hypothesis, Chase (1972), reported similarities between autistic children, children who had endured early sensory or maternal deprivation, and children with impaired vision. Furthermore, Cass (1996) confirmed, in their retrospective study of blind children, that 60% of blind children who exhibited social impairments/developmental setbacks, had experienced adverse environmental factors compared to only 23% of children with normal development outcomes. These factors included parental drug abuse, marital breakdown, and severe illness.

Children who have suffered from extreme deprivation often show similarities to autistic children. Rutter *et al.*, in 1999, examined 111 Romanian orphans who had subsequently been adopted into the United Kingdom. Researchers reported that six percent of children exhibited "quasi-autistic" behavioural patterns and another six percent demonstrated milder autistic features. Autistic-like features were most saliently observed at the age of four, and these behaviours tended to diminish over the next two years. However, autistic behaviours continued to persist in eleven children, but these children had shown greater degrees of cognitive impairments, and had endured longer periods of severe psychological privation.

The study of Romanian orphans by Rutter *et al.*, (1999) shows parallels to the origin of symptoms of autistic phenomenology that was also observed by Cass, (1996) in the blind. Therefore, the question which arises is, how does one differentiate between idiopathic autism due to organic brain abnormalities, and that of non idiopathic autism, due to extreme environmental (or sensory) deprivation (Tager-Flusberg, 2005).

Hobson (2004) suggests, that there is "not a clear boundary between blind children with autism and those with autistic [-like] features" (Hobson, 2005, pg. 15). On a theoretical level, differentiating between the origins of atypical autism in the blind, and that of sighted idiopathic autism may aid in helping to understand the phenomenology of the idiopathic autism (Hobson, 2005). But caution is required, as a blind child presenting with autistic phenomenology, regardless of origin, still requires appropriate educational interventions to manage not just their blindness, but also their autistic symptomology.

Cognitive processing differences in blind children

Some explanations for the over representation of autistic behaviours in the general blind population suggest that blind children acquire autistic phenomenology due to a different pathway, than that of sighted autistic children (Andrews & Wyver, 2005). Brambring (2008) suggests that autistic behaviours in the blind are better explained as information acquisition problems, due to the blocking of external social and communicative information, by visual loss, and that autism in sighted autistic children is more likely to be a result of deep developmental delays leading to internal information processing impairments (Brambring, 2008). Therefore, there is a clear distinction between external contributing factors to autistic phenomenology in the blind, and that of internal factors in the sighted autistic children.

The Prevalence of Autism Spectrum Disorders in children with visual loss.

The theoretical considerations of autism and blindness make it difficult to assess the accurate prevalence of Autistic Spectrum Disorders in visually impaired children, and this is further complicated by the absence of a diagnostic measure for autism in the blind and diagnostic overshadowing. Diagnostic overshadowing refers to clinician's tendency to overlook psychological and behavioural syndromes such as autism in children with intellectual disability (Reiss *et al.*, 1982). Nonetheless, large group studies have been undertaken in order to establish prevalence rates of autism in the blind. However, as these studies use children with differing aetiologies for their visual impairment, it becomes increasingly difficult to isolate the origin of autism due to sensory visual loss, from that of neurological damage.

Large group studies of assessing autism in children with visual loss

The work of Cass's (1998) retrospective study of the developmental outcome of 615 children with visual impairments has undoubtedly contributed to a greater understanding of the phenomena of autism and blindness. Cass (1998) identified two groups of children who demonstrated developmental delays. The first group acquired skills such as language and cognitive abilities; however these abilities "ceased abruptly" (31% regression in development from 16-27 months). The second group showed development of language and cognitive skills, but their social and communicative behaviours "became increasingly distorted" (Cass, 1998, p. 118). Impairments or delays in children's sensory motor understanding, verbal comprehension, expressive language (especially the presence and persistence of echolalia), increasing self-absorption and a loss of functional communication were frequently observed in the study.

Figure Seven, outlines the possible explanations for regression, and the triadic relationship between the degree of visual loss, brain abnormalities and the environment. It is hypothesised that the process of regression is switched on by environmental factors during a critical window of development in children with neurological damage and during this critical period of development, attention control and social interaction abilities emerge and develop (Cass, 1996)

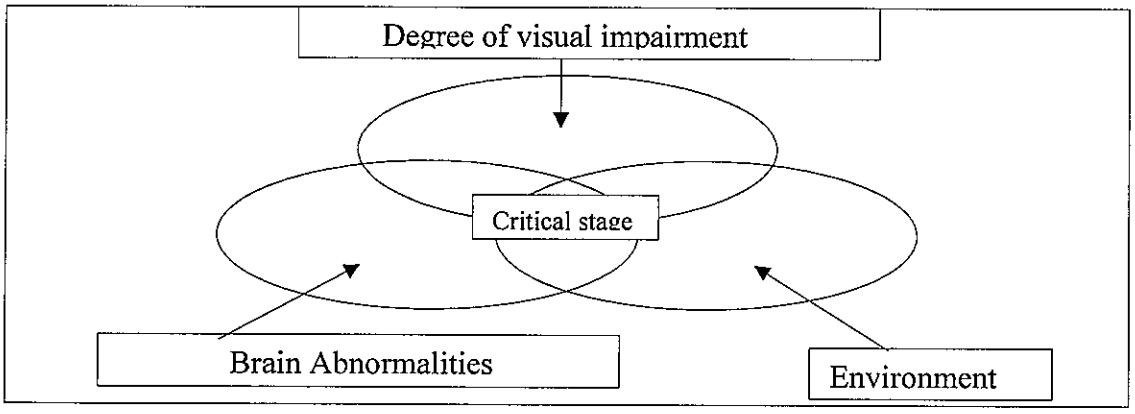


Figure Seven: Possible reasons for regression (Cass, 1996, Pg13: figure 8)

Additionally, Dale and Sonsken (2002) selected sixty-nine children from a database of 1250 children who attended the Wolfson Vision Centre in the U.K. Children were divided into three groups; profound visual impairment (PVI), profound – severe visual impairment (PVI – SVI) and severe visual impairment group (SVI), with children with PVI showing the greatest visual loss and SVI the least. Developmental profiles at the age of 10-16 months revealed that the PVI group showed more delays than did the SVI group. At 27-54 months, 16% of children showed partial delays and 17% of children showed global delays in the PVI group. In the SVI group only six out of twenty six children showed partial delays. Only five children were allocated to the PVI-SVI group and five showed partial delays between 10-16, months, and at 27-24 months one child showed partial delays and two demonstrated global delays.

The PVI group showed acceleration in expressive language skills; however deceleration was shown in verbal comprehension and sensory motor understanding. Children in the SVI group showed acceleration in learning in all three aspects of cognition. Both studies by Cass (1996) and Dale and Sonsken (2002) suggest that there is a critical period for the development of cognitive and motor skills, and early

intervention would benefit children with visual impairment. In support, Ferell *et al.*, (1998) assessed the sequence and developmental rate of 202 visually impaired children of which 60% presented with additional learning disabilities. They found that motor milestones were delayed, but expressive and receptive language was not delayed. Delays were more prevalent in children with severe visual impairments and this supports the notion that understanding of one's environment primarily occurs through vision. A lack of vision restricts the range of experiences and this has consequences in a visually impaired child's understanding of their social worlds (Dale, 2005). Table 4.1 outlines studies which have been undertaken on the prevalence of Autistic Spectrum Disorders in the blind.

Table 4.1: Research Assessing the methods used, prevalence and overall findings of research conducted assessing of Autism Spectrum Disorders in the Blind

Author(s)	Population	Methods	Prevalence	Key Findings
Norris *et al.*, (1957)	295 mixed aetiologies	Vineland Social Maturity Scale (Doll, 1936). Intern Hayes Binet Intelligence test for the blind (1952).	29% of children showed Setbacks.	Setbacks were due to extreme deprivation of appropriate experience and/or emotional disturbance. Favourable environmental opportunities were more important than medical or sociological factors in order to foster normal intelligence.
Keeler (1958)	35 RLF 18 CB 17 PNB	Developmental history and behavioural observations.	RLF; 5 children with autism and 35 children with partial autism. CB; no autism	The five children with autism displayed preference for self-isolation, delayed language, echolalia, impairments in social interaction and communicative behaviours, body rocking and smelling toys. They exhibited good memory skills and a preoccupation with music.
Chess (1971)	243 pre-school children with Rubella	Behavioural histories and behavioural observations	10 with autism 8 with partial autism	The degree of ID was related to the outcome of autism. Recovery from autistic features was seen in three children. Autism was induced by the Rubella virus and not due to sensory deprivation
Chase (1972)	246 with RLF	Parent interview Professional rating Medical history Rimland Checklist E-2	Gradient of autistic-like symptoms.	There was a clear distinction between blind children who have one or two features of autism compared to those who have the full syndrome
Fraiberg (1977)	27 children who were blind from differing aetiologies	Medical findings and birth histories and behaviour assessment	7 with autism Remainder with autistic patterns	"Ego deviation" (autism). Seven of the twenty seven cases of autism found in the study, are representative of incidence of autism in the blind population

Author(s)	Population	Methods	Prevalence	Key Findings
Rogers & Nehart- Larson (1987)	5 LCA 5 CB	Reynell Zinkin Scales of development CARS, ABC, DSM-III	5 children with LCA had autism No children with CB had autism.	Deficits in cerebellar structure may provide the neurological basis for the behavioural similarities seen in children with Leber's amaurosis and sighted autistic children.
Cass *et al.*, (1994)	102 mixed aetiologies	Retrospective hospital records collected over 15 years	Partial recovery of setback in four out of eleven children.	Severe VIs was more likely to be associated with developmental delays. Regression occurred during 15-27 months of age in children. At least, 60% of sample who showed setback had suffered social adversity in comparison to 23% of children who had developed normally. Increased stereotypes prevented learning.
Goodman & Minne (1995)	17: 5 LCA, 4 Norries Disease, 3 SOD, 5 other	ABC	4 PDD	Screening questionnaires have a useful role in only locating PDDs, but the ADI (Le Couteur *et al*, 1989) is more useful.
Brown *et* al., (1997)	24 with CB	DSM-IIIR	42% with autism	(a)Autistic features more prevalent in the blind (b) overlap in symptomology
Elk *et al.*, (1998)	27 ROP 4 with HB	Griffiths Developmental Scales (Alin-Akerman & Nordberg,1980) and CARS	15 ROP with autism (all had ID and one-third cerebral palsy) 2 HB autism	Strong association between ROP and autistic disorder. The association is most probably mediated by brain damage and is largely independent of the blindness per se.

Author(s)	Population	Methods	Prevalence	Findings
Hobson *et al.*, (1999)	9 children with CB. 9 =sighted autistic children	CARS BCDP DSM-III-R	1/3 impaired; relating to people, emotional response, sensory	Substantial similarities were reported between the groups, but also group differences, specifically in the domain of social-emotional responsiveness.
Hobson & Bishop (2003)	18: 8 with ROP 4 LA and 6 other	CARS and playground observations	socially engaged (MS) socially impaired group (LS)	Socially impaired blind children demonstrated limited reciprocal engagement with others.
Fazzi, Rossi, Signorini, Rossi, Bianchi & Lanzi (2007)	24, (13 males, 11 females)	Modified CARS-- excluding item VII Visual Responsiveness	Four scored above cut-off for the presence of autism	Visually impaired children are at risk during their early interactive experiences, which may be affected by their inability to connect with others.
Mukaddes, Kilincaslan, Kucukyazici, Sevketogl & Tuncer(2007)	257 blind children and and adolescents	ABC, direct observation and DSM-IIIR	30 presented with autism	Autism is more prevalent in individuals with greater neurological impairments and severe visual impairment compared to individuals who are only blind.

Adapted from Carvil and Marston (2002) **Eye conditions**: Congenital Blindness (CB); Postnatal Blindness (PNB); Leber Congenital Amaurosis (LCA); Visual Impairment (VI); Retinopathy of Prematurity (ROP); Hereditary Blindness (HB), Septo-Optic Dysplasia (SOD) and, Retrolental Fibroplasia (RLF). **Developmental Descriptors**: Pervasive Developmental Disorders (PDD), Intelligence Quotient (IQ), Intellectual Disability (ID). **Developmental Assessments**: Autism Behaviour Checklist (ABC), Diagnostic and Statistical Manual of Mental Disorders (DSM-III & DSM-III-R), Autism Diagnostic Interview (ADI), Behaviour Checklist for Disordered Preschoolers (BCDP) and Childhood Autism Rating Scale(CARS).

Autism in children with Optic Nerve Hypoplasia and Septo Optic Nerve Hypoplasia

The fundamental problem of assessing autistic disorders in children with Optic Nerve Hypoplasia and Septo Optic Nerve Hypoplasia is the uneven cognitive and behavioural profiles that children present, as a consequence of the differing degrees and combinations of associated hormonal loss, midline malformations and/or visual impairments. For instance, during a small cohort study of thirteen children with Septo Optic Dysplasia and Optic Nerve Hypoplasia, Ek, Fernell and Jocobson (2005) reported that autistic disorders had been diagnosed in six of the thirteen children, and that an autistic-like condition was found in another three children. However, eight children had cognitive capacities within the normal or near-normal range, and five children had varying degrees of intellectual disability, but autism, or an autistic-like condition, was diagnosed in all of these cognitive sub-groups.

Children also demonstrated severe mood swings, and temper tantrums, during their first year of infancy and, later in life, sluggish tempos, low tolerance to frustration, and a narrow range of interests were often observed by parents. Interestingly, all children spoke fluently, and twelve had started to talk at the expected age, but clear impairments in their communicative ability was documented.

In a larger questionnaire study concerning the musical abilities of children with Septo Optic Dysplasia and Optic Nerve Hypoplasia, Pring and Ockelford (2005) reported in their demographic data, that six children from the cohort of nineteen children had been diagnosed with autistic disorders (9%). However, it is not known

what the severity of intellectual disability, or the degree of visual acuity was for these nine children.

Commonly associated behavioural traits indicative of autistic symptomology in sighted children have also been identified in children with Septo Optic Dysplasia and Optic Nerve Hypoplasia. These include moderate to severe delays in information processing, tactile and auditory defensiveness, difficulty with transitions, (Bahar *et al.*, 2003). Specifically, Bahar *et al.*, (2003) reported that children with Septo Optic Dysplasia and Optic Nerve Hypoplasia show impairments in the triad of impairments (Wing & Gould, 1979) which include, avoiding social interaction, engaging in atypical language development, and a rigid adherence to routines. Bahar *et al.*, (2003) concluded that some of the delays seen were not typically observed in other groups of blind children, with different aetiologies for their visual impairment.

Most recently, Parr, Shaffer, Salt and Dale (2008), reported high incidences of autistic-like phenomenology, and behavioural difficulties from the retrospective analyses of medical reports of sixty-nine children with Optic Nerve Hypoplasia and Septo Optic Dysplasia. In this study, at least 46% of children showed an impairment in one domain of the triad of impairments, and 22% of children displayed impairments in all three domains. Children with a profound visual impairment were more likely to experience impaired social communication and show repetitive behaviours. When Parr *et al.*, (2008) controlled for levels of visual impairment, children with autistic disorders were more developmentally delayed, specifically in their verbal communication and expressive language abilities.

Summary of the aims of Chapter Four

Taking into consideration the theoretical and methodological issues of assessing autism in children with visual impairments, the psychometric properties of the adapted Autism Diagnostic Observation Schedule needed to be initially considered prior to the systematic measurement of autistic disorders in children with Septo Optic Dysplasia, Optic Nerve Hypoplasia and isolated Hypopituitarism.

Therefore, the aims of Chapter Four are too;

- Investigate the psychometric properties of the Autism Diagnostic Observation Schedule, in comparison to the Social Communication Questionnaire, the Gilliam Autism Rating Scale and Clinician diagnosis, for children with Septo Optic Dysplasia, Optic Nerve Hypoplasia and isolated Hypopituitarism.
- Assess the types, and incidences of autistic behaviours in the closely related syndromes of Septo-Optic Dysplasia and Optic Nerve Hypoplasia, in comparison to children with isolated cases of Hypopituitarism. This will help to identify whether hormonal loss, visual loss, and/or intellectual disability better account for autistic phenomenology within these conditions.

4.5 Methods

Recruitments of participants

Prior to information packs being sent to families, ethical approval was sought, and granted from the National Research Ethics Services (NRES). Information packs consisting of an adult and child invitation sheet outlining the research aims and

objectives, consent forms and a pre-paid envelope (Appendix, D) were sent to prospective families through the following avenues;

(i) Children with the three diagnoses were identified for recruitment via a computer database of patients held at the Birmingham Children's Hospital's Endocrinology Department. In total, twenty-five children with Septo Optic Dysplasia, twenty-eight children with Optic Nerve Hypoplasia and twenty children with isolated Hypopituitarism were invited to participate. The information packs were sent to the families concerned by the secretaries of Dr J. Kirk, Consultant Endocrinologist at the Birmingham Children's Hospital's Endocrinology Department.

(ii) Children with Septo-Optic Dysplasia and Optic Nerve Hypoplasia were also invited to participate through the Focus Family charity conference held in February 2005 in Oxford (Abingdon). Invitation packs were sent out by the national charity "Look" who identified eighteen children with Septo-Optic Dysplasia and thirty-five Children with Optic Nerve Hypoplasia on their national database. The National Blind Children's Society also identified seventeen children with Septo-Optic Dysplasia and twenty-two children with Optic Nerve Hypoplasia on their national database. Information packs were sent out by sectaries at the charities.

(iii) Lastly an advertisement about the study was placed on a web page for the Pituitary Foundation (http://www.pituitary.org.uk/content/view/310/105/. Parents who showed an interest in the study through the Pituitary

Foundation contacted the researcher directly through the web page, who then forwarded the information packs on to the contact details provided. In addition, the charity the "UK Child Growth Foundation" sent out four information packs to families who had isolated Hypopituitarism.

Inclusion criteria for participants

Children between the ages four to fifteen years of age at the time of testing were contacted. Children who had a confirmed diagnosis of one of the three syndromes in question and no other associated syndromes were only approached. It was understood, however, that children with epilepsy, diabetes insipidus, developmental delay or other conditions associated with the three syndromes would be included. This ensured that the sample characteristics of participants of the thesis were closely representative of the syndrome population in the U.K at the present time.

Participants

Characteristics of the Septo Optic Dysplasia group

Thirty-two participants returned the consent form. Two patients withdrew from the study by phone, after the questionnaire pack had been received. One further participant provided insufficient contact details, and another participant moved addresses during the initial recruitment stages of the research. Of the remaining twenty-eight participants, twelve were female and sixteen were male. The mean age in years of this group was 9.6 (SD: 34.5; range 4.2-16.0 years). Twelve participants were registered blind, of which three had some light perception, the reminder of children exhibited varying levels of visual impairments from mild to moderate. Three

participants demonstrated a moderate to severe visual impairment, and in eight participants, visual function was categorised as normal to a mild impairment. Three children were partly able, one child needed partial help with walking and two used wheelchairs for mobility. The Age Behaviour Composite Equivalence mean score (as determined by the Vineland Adaptive Behaviour Scale: Sparrow, Balla & Ciccetti, 1987, see Methods section Measures) was 76.74 months (SD = 47.74) and Expressive Language Skill Score (as determined by the Vineland Adaptive Behaviour Scale: Sparrow *et al.*, 1984) was 97.88 months (SD= 54.88).

Optic Nerve Hypoplasia group

Fifteen participants returned the consent form. One patient withdrew from the study due to health reasons mid-way through the study, but had completed the questionnaire pack. Six of the remaining fourteen participants were female and eight were male, their mean age was 7.83 years (SD: 37.48; range: 4.8-12.2 years). The level of visual acuity ranged from, two children being registered blind, two children who had a severe visual impairment and the remainder exhibited various levels of visual function from a mild to a moderate impairment. Two children were partly able, and both required partial help with walking but not wheelchair use. The Age Behaviour Composite Equivalence mean scores (as determined by the on the Vineland Adaptive Behaviour Scale: Sparrow *et al.*, 1984) was 87.23 months (SD = 57. 51) and Expressive Language Skill score (as determined by the Vineland Adaptive Behaviour Scale: Sparrow *et al.*, 1984) was 79.15 months (SD= 69.01).

Hypopituitarism group

Fifteen participants returned the consent form; however, one participant was excluded due to co-morbidity with other clinical syndromes. Of the remaining fourteen participants four were female and ten were male, and the mean age was 11.1 (SD: 46.1; Range: 5.2-16 years of age) and visual function was normal. The Age Behaviour Composite Equivalence mean score (as determined by the on the Vineland Adaptive Behaviour Scale: Sparrow *et al.*, 1984) was 89.88 months (SD = 52. 88) and the Expressive Language Skill score (as determined by the Vineland Adaptive Behaviour Scale: Sparrow *et al.*, 1984) was 133.86 months (SD= 53.54).

Individual participant characteristics for each syndrome are presented in tables 4.51-4.53. Participant characteristics describe each child's chronological age, gender, level of visual loss (LP= light perception and AS = Astigmatism), Adaptive Behaviour Composite level and the reported presence (+) or absence (-) of Autism Spectrum Disorders according to the screening or diagnostic scales used to assess Autistic Spectrum Disorders.

Table 4.5.1: Child demographics for children with isolated cases of Hypopituitarism

Participant Number	Diagnosis	Chronological Age (months)	Gender	Vision	ABC Level	SCQ	GARS	ADOS	Clinician
1	Hypopituitarism	65	Male	Normal	Adequate	–	–	–	–
2	Hypopituitarism	170	Female	Normal	Moderately Low	–	–	–	–
3	Hypopituitarism	172	Female	Normal	Mild	–	–	–	–
4	Hypopituitarism	160	Female	Normal	Adequate	–	–	–	–
5	Hypopituitarism	109	Male	Normal	Moderately High	–	–	–	–
6	Hypopituitarism	166	Male	Normal	Adequate	–	–	–	–
7	Hypopituitarism	115	Male	Normal	Adequate	–	–	–	–
8	Hypopituitarism	79	Male	Normal	Adequate	–	–	–	–
9	Hypopituitarism	158	Male	Normal	Adequate	–	–	–	–
10	Hypopituitarism	72	Male	Normal	Moderately Low	–	–	–	–
11	Hypopituitarism	192	Male	Normal	Mild	–	–	–	–
12	Hypopituitarism	192	Male	Normal	Adequate	–	–	–	–
13	Hypopituitarism	78	Female	Normal	Adequate	–	–	–	–
14	Hypopituitarism	146	Male	Normal	High	–	–	–	–

Table 4.5.2: Child demographics for children with Optic Nerve Hypoplasia (ONH)

Participant Number	Diagnosis	Chronological Age (months)	Gender	Vision	ABC Ability	SCQ	GARS	ADOS	Clinician
15	ONH	72	Male	Severe	Mild	-	-	-	-
16	ONH	107	Male	Impaired	Severe	+	-	-	-
17	ONH	103	Male	Severe	Severe	-	-	-	-
18	ONH	125	Male	Profound	Moderate	+	-	+	+
19	ONH	36	Male	Impaired	Moderately High	-	-	-	-
20	ONH	80	Male	Profound (LP)	Severe	+	+	+	+
21	ONH	80	Female	Impaired (AS)	Adequate	-	-	-	-
22	ONH	57	Female	Severe	Moderate	+	+	+	-
23	ONH	192	Male	Severe	Profound	+	+	+	+
24	ONH	70	Female	Impaired	High	-	-	-	-
25	ONH	102	Female	Impaired	High	-	-	-	-
26	ONH	110	Female	Impaired	High	-	-	-	-
27	ONH	112	Male	Impaired	Adequate	-	-	-	-
28	ONH	69	Female	Impaired	Adequate	-	-	-	-

Table 4.5.3: Child demographics for children with Septo Optic Dysplasia (SOD)

Participant Number	Diagnosis	Chronological Age (months)	Gender	Vision	ABC Ability	SCQ	GARS	ADOS	Clinician
28	SOD	50	Male	Profound	Mild	+	+	+	+
29	SOD	68	Male	Profound (LP)	Adequate	+	-	-	-
30	SOD	83	Female	Impaired	Adequate	-	-	-	-
31	SOD	84	Male	Impaired	Adequate	+	+	+	+
32	SOD	102	Female	Impaired	Adequate	+	-	+	+
33	SOD	108	Female	Impaired	High	+	+	+	-
34	SOD	110	Female	Severe	Mild	-	-	-	+
35	SOD	120	Female	Severe (AS)	Mild	+	+	+	+
36	SOD	121	Male	Severe (AS)	Mild	-	+	-	-
37	SOD	132	Female	Impaired	Mild	+	+	+	+
38	SOD	135	Male	Severe	Mild	-	-	+	-
39	SOD	145	Male	Severe	Mild	+	+	+	+
40	SOD	149	Male	Profound (LP)	Mild Deficit	+	+	-	-
41	SOD	156	Male	Profound	Moderately Low	+	+	+	-
42	SOD	84	Male	Profound	Moderately Low	+	-	-	-
43	SOD	162	Male	Severe (AS)	Moderately Low	+	-	+	-
44	SOD	89	Female	Profound	Moderate	-	-	-	-
45	SOD	90	Female	Impaired	Moderate	-	-	+	-
46	SOD	106	Female	Profound	Moderate	-	-	-	-
47	SOD	108	Male	Severe	Moderate	-	-	-	-
48	SOD	101	Male	Profound	Moderate	+	+	+	+

49	SOD	151	Female	Profound	Moderate	+	+	-	-
50	SOD	192	Female	Profound	Moderate	+	-	+	-
51	SOD	141	Female	Impaired	Profound	+	-	+	+
52	SOD	61	Male	Profound	Severe	-	-	-	-
53	SOD	63	Male	Severe	Severe	+	-	+	+
54	SOD	89	Male	Impaired	Severe	+	-	-	-
55	SOD	50	Male	Profound	Moderate	+	-	-	-
56	SOD	48	Male	Profound	Mild	+	+	+	+

Measures

Demographic Data

Parents were asked during the Vineland Adaptive Behaviour interview about their children's level of visual acuity. Children's level of vision was grouped accordingly as; mild, moderate, severe (including astigmatism), some light perception or totally blind

Autism Diagnostic Observation Schedule

The Autism Diagnostic Observation Schedule (ADOS; Lord *et al.*, 2002) is a semi-structured standardised assessment of communication, social interaction and play or imaginative use of materials. Previous research has shown that impairments in these behavioural domains are crucial indicators of suspected autistic tendencies in children (Lord *et al*, 1998). The schedule also examines speech abnormalities, stereotyped and restricted interests. However, the Autism Diagnostic Observation Schedule does not utilize impairments in these areas for diagnosis of autism, mainly because these behaviours frequently occur in children with learning disabilities and/or visual impairments.

The Autism Diagnostic Observation Schedule consists of four modules, each of which is appropriate for individuals who differ in developmental ability and language acquisition, ranging from no expressive language to some receptive language to verbally fluent. Each module consists of planned social situations referred to as "presses" in which a range of social initiations and responses are likely to appear from the child. Communication between the examiner and the child is intended to elicit a range of

communicative interchanges. Play situations allow the examiner to observe a range of imaginative activities and social role-play sequences by the child. The Autism Diagnostic Observation Schedule aims to elicit spontaneous behaviours in standardised contexts for children from the age of three up to adulthood.

Module one, is intended for individuals who do not consistently use phrase speech (defined as non-echoed, three-word utterances that sometimes involve a verb and that are the child's spontaneous, meaningful word combinations). Module two is a combination of the Autism Diagnostic Observation Schedule and Pre- Linguistic Autism Diagnostic Observation Schedule and is intended for individuals with some phrase speech who are not verbally fluent.

Module three, is intended for children for whom playing with toys is age-appropriate, (usually under twelve - sixteen years of age) who are verbally fluent. Verbal fluency is broadly defined as having the expressive language of a typical four year-old child who can produce sentences, grammatical forms, use language to provide information about events out of context and produce some logical connections within sentences (e.g., "but" or "though"). Module four includes the socio-emotional questions and further interview items and is intended for verbally fluent adolescents and adults. The difference between Modules three and four lies primarily in whether information about social-communication is more appropriately acquired during play or a conversational interview.

Modules one and two are usually conducted while moving between different places around a room, reflecting the interests and activity levels of young children or

children with very limited language; Modules three and four take place sitting at a table and involve more conversation and language without a physical context.

The selection of the appropriate module for the individual is based on the child's expressive language skills that can be determined by the Vineland Adaptive Behaviours Scales (VABS; Sparrow *et al.*,) and the child's chronological age. Each module is videotaped and the assessment lasts between thirty to forty-five minutes. The experimenter scores the schedule immediately after it has been administered and makes notes during the assessment.

The Autism Diagnostic Observation Schedule was modified to take into account children's visual impairments. Toys that rely heavily on visual stimulation were substituted for toys that were more tactile and auditory in nature, but these changes still aimed to measure the same behaviours as the original Autism Diagnostic Observation Schedule toys. A catalogue produced by the Royal National Institute of the Blind (RNIB) provided a selection of toys suitable for blind and partially sighted children for substitutions (Refer to Chapter Three).

The Social Communication Questionnaire (SCQ; Rutter, Bailey, Berument, LeCouteur, Lord & Pickles, 2003)

The Social Communication Questionnaire (SCQ; Rutter, *et al.*, 2003) is a brief instrument that helps to evaluate communication skills and social functioning in children who may have autism or Autistic Spectrum Disorders. It is completed by a parent or other primary caregiver in less than ten minutes. It comprises forty yes-or-no questions. There are two versions of the Social Communication Questionnaire. Firstly,

the Lifetime Form focuses on the child's entire developmental history, providing a total score that is interpreted in relation to specific cut-off points. Moving from developmental history to present status, the Current Form looks at the child's behaviour over the most recent three-month period.

The Social Communication Questionnaire is based on the original Autism Diagnostic Interview - Revised (ADI-R) which itself is based on the algorithms used for diagnosis for autism according to the ICD-10 and DSM-IV. A score of one is given for the presence of an abnormal behaviours and a score of zero is given if the behaviour is absent. Thus, total scores range from zero to thirty-nine for children with language and total scores ranges of zero to thirty for children without language and most individuals with autism have a Social Communication Questionnaire scores above fifteen. The Social Communication Questionnaire scores of children with specific or general learning disabilities are usually substantially above the general population but below those for children with PDDs, hence the Social Communication Questionnaire discriminates between children with PDD and other developmental disorders (Berument *et al.*, 1999).

Gilliam Autism Rating Sale (GARS; Gilliam, 1995)

The Gilliam Autism Rating Scale (GARS; Gilliam, 1995) helps to identify and diagnose autism in individuals from the age of three through to twenty-two years of age. Items on the Gilliam Autism Rating Scale are based on the definitions of autism adopted by the Autism Society of America and the Diagnostic and Statistical Manual of

Mental Disorders. The items are grouped into four subtests: stereotyped behaviours, communication, social interaction, and developmental disturbances.

The Gilliam Autism Rating Scale has strong psychometric characteristics that were confirmed through studies of the test's reliability and validity by Gilliam in 1995. Coefficients of reliability (internal consistency, test retest, and interscorer) for the subtests are all in the .80s and .90s. The GARS is the only test for autism that reports data for all three kinds of reliability. The validity of the GARS was demonstrated by confirming that: (a) the items of the subtests are representative of the characteristics of autism; (b) the subtests are strongly related to each other and to performance on other tests that screen for autism; and (c) the Gilliam Autism Rating Scale performance discriminates persons with autism from persons with other severe behavioural disorders such as emotional disturbance, speech and language disorders and other conditions.

Clinician diagnosis

For those children who attended, and were recruited through the Birmingham Children's Hospital, a Clinician's diagnosis of Autistic Spectrum Disorders was retrieved from the Birmingham Children's Hospital Endocrinology department database by a research nurse after the study had been completed. Children who were recruited from charities provided information about the presence of developmental disorders (i.e. autism) through the Gilliam Autism Rating Scale (GARS: Gilliam, 1995) sub-section; VI of Key questions, and this information was only looked at after the study finished, however, some parents disclosed this information during the Autism Diagnostic Observation Schedule assessment or the Vineland Adaptive Behaviour Schedule

interview. The key questions asked for information about where, and by whom, the diagnosis of autism was given, and this was mostly through by a medical professional or Clinical Psychologist at the Hospital that patients attended for their routine care.

Vineland Adaptive Behaviours Scales (VABS; Sparrow et al., 1984)

To select an appropriate module of the Autism Diagnostic Observation Schedule to give to children, parents were interviewed on the Vineland Adaptive Behaviours. The Vineland Adaptive Behaviours Scale is a structured interview which measures the four domains of adaptive functioning which contribute to establishing the presence of intellectual disability; these domains include the Communication domain, with the sub-domains of Receptive language, Expressive language and written skills. The second domain, Daily Living Skills, includes the sub- domains of Personal, Domestic and Community skills and the third domain, Socialisation skills, includes the sub-domains of; Interpersonal relationships, Play and Leisure, and Coping Skills.

The interview schedule has demonstrated strong psychometric properties with Pearson correlation coefficients for test re-test reliability ranging from 0.98 to 0.99. Inter-rater reliability was between 0.62 to 0.78 for the Domains and 0.74 for the Adaptive Behaviour Composite. Criterion related validity yielded a correlation of 0.97 in a sample of adults with intellectual disability.

Procedure

Questionnaire packs which included the Social Communication Questionnaire and Gilliam Autism Rating Scale were completed by parents/guardians of the children. Following the completion of the questionnaire pack, the Vineland Adaptive Behaviour

Scale interview was completed over the telephone or in person at the caregiver's home if they lived within the West Midlands area, in order to ascertain which Autism Diagnostic Observation Schedule module was appropriate to administer to children.

Within the information pack, parents were asked to provide contact details of the school their child attended. Schools were then sent an information pack about the study and a Criminal Reference Bureau check of the researcher. Schools were contacted within three to seven days of receipt of this letter (parents were also copied into the letter and sent a copy). Once a suitable date had been arranged, a letter was sent to parents to notify them of the date of the visit and this information was followed up by a telephone call the day before the visit.

All Autism Diagnostic Observation Schedule assessments were recorded in a quiet room and were video recorded using a Sony Video camera. The fourteen blind children received the adapted version of the Autism Diagnostic Observation Schedule which took into consideration their visual loss and the remainder of children were given the standardised version the Autism Diagnostic Observation Schedule. Assessments were scored immediately after administration, and further re-analysed and transferred onto DVD or videocassette tapes in a video editing suite located at the Developmental Psychology department at the University of Birmingham.

Data Analysis Strategy

Exploratory analyses were initially conducted to establish whether data met parametric assumptions. Shapiro–Wilk W tests revealed no statistically significant differences on the Total Score and Domain Scores of the Autistic Diagnostic

Observation Schedule, the Communication and Social interaction sub domain of the Social Communication Questionnaire, or the Total Score of Social Communication Questionnaire for the overall participant group (N=56), which lead to the overall assumption that the distribution was normal.

To evaluate the psychometric properties of the measures used to assess and identify Autism Spectrum Disorders, the validity was firstly considered. The concurrent validity between the three scales, and clinical diagnosis was examined using Pearson correlation coefficients. To assess agreement between the three scales used, and clinician diagnosis; univariate pair-wise analysis was employed based on Cohen's Kappa. The discriminating validity of the Autism Diagnostic Observation Schedule, Social Communication Questionnaire, and the Gilliam Autism Rating Scale was measured against the Clinician classification for Autistic Spectrum Disorders, and against non-diagnosis of Autism Spectrum Disorder, through the use of the receiver operating characteristics (ROC) curve.

Exploratory analyses were initially conducted to establish whether data met parametric assumptions. Shapiro–Wilk W tests revealed statistically significant differences on the Total Score and Domain Scores of the Autistic Diagnostic Observation Schedule, the Communication and Social interaction sub domain of the Social Communication Questionnaire, but not the Total Score of Social Communication Questionnaire, which lead to the overall rejection of the assumption that the distribution was normal. Subsequent Levene's tests confirmed that the data's homogeneity of variance was also violated. Furthermore, outliers were identified in the group of

children with isolated Hypopituitarism and Optic Nerve Hypoplasia and the number of children per syndrome group was also uneven, hence non-parametric tests were used.

Firstly, Exploratory Data Analysis (EDA) looked at the percentage of children scoring above the cut-off for Autistic Spectrum Disorders occurring in children with isolated Hypopituitarism, Optic Nerve Hypoplasia and Septo Optic Dysplasia. The percentage and number of children scoring above the suggested cut-off for Autistic Spectrum Disorders according to module selection of the Autism Diagnostic Observation Schedule using Chi-Squared tests was analysed.

To assess for differences between child syndrome groups, a series of non-parametric Kruskal–Wallis were used on the raw scores of Autism Diagnostic Observation Schedule and the Social Communication Questionnaire Total scores and sub-domains scores of Reciprocal Interaction and Communication. Post-hoc pair wise analysis using Mann–Whitney *U*-tests identified where differences lay between the child syndrome groups.

Level of visual acuity and level of intellectual disability were explored with a series of non-parametric Kruskall–Wallis analyses on the raw scores on the Autism Diagnostic Observation Schedule, Social Communication Questionnaire Total score and the sub domains scores of Reciprocal Interaction and Communication for children with Optic Nerve Hypoplasia and Septo Optic Dysplasia only.

Children were grouped according to their level of visual acuity as; (1) mild to moderate visual loss (2) Severe visual loss (including astigmatism) (3) Profound visual loss (complete visual loss or light perception). Children were also grouped according to their level of ability as; (1) above average/average (2) mild – moderate (3) severe (4)

profound intellectual disability. To avoid Type I errors, Bonferroni corrections to the significance level of statistical tests were used when multiple comparisons were used.

Lastly, a follow-up linear regression analysis was conducted to predict whether level of visual acuity, or intellectual disability, contributed to Autistic Spectrum Disorders, Atkin and West (1996) stated that linear regressions could be used on non-normal populations, and therefore could be applied to the present data set.

4.6 Results

Assessing the agreement, and relationship between, the Autism Diagnostic Observation Schedule (ADOS-G), Social Communication Questionnaire (SCQ), the Gilliam Autism Rating Scale (GARS), and Clinician diagnosis.

The concurrent validity between the three scales was assessed at the total and sub-domain levels of Social Interaction and Communication for the ADOS, SCQ and GARS. Table 4.6.1 presents the Pearson correlation coefficients between the three scales. Generally, Pearson correlation coefficients between; 0 to 0.2 are considered weak, 0.3 to 0.6 to moderate and 0.7 to 1.0 strong.

Table 4.6.1: Pearson correlation coefficients for correlations for the SCQ, GARS and ADOS at total score, communication, and reciprocal social interaction domain score levels.

		Total Score			Social Interaction			Communication		
		SCQ	GARS	ADOS	SCQ	GARS	ADOS	SCQ	GARS	ADOS
Total Score	SCQ									
	GARS	.55**								
	ADOS	.64**	.49**							
Social Interaction	SCQ	.92**	.70**	.73**						
	GARS	.70**	.74**	.39**	.68**					
	ADOS	.73**	.39**	.65**	.69**	.37**				
Communication	SCQ	.89**	.54**	.55**	.70**	.45**	.54**			
	GARS	.67**	.69**	.46*	.67**	.73**	.43**	.49*		
	ADOS	.69**	.54**	.89**	.70**	.49**	.85**	.49*	.53**	

***p < 0.01*

Analysis revealed that the Autism Diagnostic Observation Schedule was significantly correlated with the Social Communication Questionnaire at total and social interaction. However, the Gilliam Autism Rating Scale and Social Communication Questionnaire both showed the same moderate degree of correlation with the Autism Diagnostic Observation Schedule at the sub-domain level of communication.

Agreement between clinician diagnosis and instruments used to measure Autism/Autism spectrum disorders.

To assess agreement between the three scales used, and Clinician diagnosis; univariate pair-wise analysis was employed based on Cohen's Kappa. There was good agreement for the diagnosis of Autism Spectrum Disorders between Clinician diagnosis

and the Autism Diagnostic Observation Schedule cut-off (Kappa=0.60), although the agreement between Clinician diagnosis and the Social Communication Questionnaire cut-off point was moderate (Kappa = 0.46). However, the agreement between Clinician diagnosis and the Gilliam Autism Rating Scale cut- off point for Autism, was reported to be low (Kappa = 0.39).

Furthermore, agreement between the three scales used for the present thesis was also examined. The Social Communication Questionnaire and the Autism Diagnostic Observation Schedule showed good agreement (Kappa = 0.62), the Autism Diagnostic Observation Schedule and Gilliam Autism Rating Schedule agreement was fair (Kappa = 0.44), and agreement between the Gilliam Autism Rating Schedule and the Social Communication Questionnaire was also shown to be fair (Kappa = 0.50).

Even though good agreement levels were achieved, 36% of participants who reached the cut-off for Autism Spectrum Disorders on the Autism Diagnostic Observation Schedule did not receive a diagnosis of Autism from a Clinician. Furthermore, 20% of individuals who reached the cut-off point for Autism on the Social Communicative Questionnaire did not receive a diagnosis of Autism from a Clinician.

Additionally, 26% of participants who met the cut off point for Autism Spectrum Disorders on the Social Communicative Questionnaire did not meet the cut off point on the Autism Diagnostic Observation Schedule. For these reasons, the use of these scales should be interpreted with caution when not supported by a diagnosis of Autism from a Clinician experienced in Autism and/or visual impairments. The participant demographic table 4.5.1-4.53 summarises the diagnostic classification for each child according to Clinician Diagnosis, scoring above the cut-off point for Autism

Spectrum Disorders on the Social Communicative Questionnaire, the Gilliam Autism Rating Scale and the Autism Diagnostic Observation Schedule.

Of the fifty-six children who were evaluated on all three measures for Autistic Spectrum Disorders, twenty-four children met the criteria for further investigation of pervasive developmental disorders using the Social Communicative Questionnaire, eighteen met the criteria for autism using the Autism Diagnostic Observation Schedule, and fourteen met the criteria for Autism Spectrum Disorders according to the Gilliam Autism Rating Scale. Furthermore, fourteen children received Clinician diagnosis, which reiterates the disparity of reporting of Autism Spectrum Disorders amongst children.

Predictive power, sensitivity and specificity of Clinician diagnosis against the three instruments used to measure Autism/Autism spectrum disorders

The discriminating validity of the Autism Diagnostic Observation Schedule, Social Communication Questionnaire, and the Gilliam Autism Rating Scale was measured against the Clinician classification for Autism Spectrum Disorders, and against non diagnosis of Autism Spectrum Disorder, through the use of the receiver operating characteristics (ROC) curve. The ROC curve is a commonly employed statistical tool used to compare the validity of differing diagnostic tools, which measure a specific clinical condition (Bruns, Huth, Magid & Young, 2000).

The area under the curve (AUC) for children receiving a diagnosis from a Clinician of Autism Spectrum Disorders was identified as a dependent variable, and scoring above the Autism Diagnostic Observation Schedule cut-off point for Autistic

Spectrum Disorder, the Social Communication Questionnaire and the Gilliam Autism Rating Scale cut-off point for Autism were plotted as the independent predictor. The area under the curve (AUC) measures the overall predictive validity of the instrument against diagnosis and non diagnosis by a "gold standard" which in this case is Clinician diagnosis, where an AUC value of = .50, signals random predication, 0.60 < AUC 0.70 ≤ poor, 0.70 <, AUC, ≤ 0.80 fair, 0.8 < AUC ≤ 0.90 good, and AUC >90 excellent validity (Tape, 2000).

Table 4.6.2 shows that the area under the curve revealed that the Autism Diagnostic Observation Schedule, showed "good" predictive value, the Social Communication Questionnaire showed "fair" predictive value; however, the Gilliam Autism Rating Scale predictive value was reported as borderline "poor".

Table 4.6.2: The area under the curve; the positive predicative value of instruments, against clinician diagnosis of Autism Spectrum Disorders.

Area Under Curve (AUC)	95% Confidence Interval	
	Lower	Upper
SCQ = 75.8%	67.7% &	83.9%
GARS = 69.1%	59.4% &	78.9%
ADOS = 83.8%	76.8% &	90.9%

Using the clinician diagnosis as the "gold standard" for assessing Autistic Spectrum Disorders the sensitivity and specificity for diagnosing autism was calculated for each of the measures explored. Methods for estimating ROC curves rely on the

existence of a gold standard that dichotomizes patients into having a disorder that is "present" or "absent" (Obuchowski, 2006). However, as there is yet to be an assessment that allows for the testing of autism in the visually impaired, Clinician diagnosis was selected as the "gold standard" as this is the only protocol that is currently employed. Sensitivity measured the proportion of true positives that were correctly identified and Specificity measured the proportion of true negatives that were correctly identified. Sensitivity and Specificity measures the diagnostic ability of the tests and thus its validity (Altman & Bland, 1994).

The ROC co-ordinated curve was used to assess the sensitivity of the Autism Diagnostic Observation Schedule, which reached 0.91, Social Communication Questionnaire that also achieved 0.91, and the Gilliam Autism Rating Scale sensitivity only reached 0.59. In addition, the Social Communication Questionnaire specificity was 0.34, the Autism Diagnostic Observation Schedule was 0.24 whereas, the specificity of the Gilliam Autism Rating Scale reached 0.20. The ROC analysis showed that the Autism Diagnostic Observation Schedule and the Social Communication Questionnaire were more effective in measuring Autistic Spectrum Disorders in than was the Gilliam Autism Rating Scale.

Comparison of Autistic Spectrum Disorders according to the clinical syndromes of Isolated Hypopituitarism, Optic Nerve Hypoplasia and Septo Optic Dysplasia

Table 4.6.3 shows that children with Septo-Optic Dysplasia had more reported cases of Autistic Spectrum Disorders than children with Optic Nerve Hypoplasia. No children with isolated Hypopituitarism reported incidences of autistic disorders.

Table 4.6.3: Percentage of children with isolated Hypopituitarism, ONH and SOD scoring above the suggested cut-off point for Autistic Spectrum Disorders on the SCQ, ADOS or receiving a diagnosis of Autism from a Clinician.

Diagnosis N	Clinician	SCQ	ADOS
Isolated Hypopituitarism (N=14)	0.0%	0.0%	0.0%
Optic Nerve Hypoplasia (N=14)	21.4%	33.3%	28.6%
Septo Optic Dysplasia (N=28)	35.7%	67.9%	46.4%

Reporting of Autistic Spectrum Disorders according to module selection on the Autism Diagnostic Observation Schedule

There was a significant difference between the percentage of children who scored above the cut- off point for Autistic Spectrum Disorders on module one and module two compared to children who were administered module three and four of the ADOS (χ^2=23.90: $df = 1$, $p < 0.01$) across all syndrome groups. The percentage and number of children scoring above the cut-off point for Autistic Spectrum Disorders is summarised in table 4.6.4.

Table 4.6.4: The percentage and number of children who were given module one, two, three or four who scored above the suggested cut-off point for ASD on the Autism Diagnostic Observation Schedule.

% and Number of children Scoring above cut-off point on ADOS for ASD	Module Selection			
	1	**2**	**3**	**4**
N (=56)	(14)	(2)	(24)	(16)
% of children with Autistic Spectrum Disorders	69%	100%	12.5%	29%
Number of children with Autistic Spectrum Disorders	9	2	4	3

Comparison of raw scores on the Autism Diagnostic Observation Schedule between participant groups

To explore the statistical differences for the severity of autistic symptomology between syndrome groups on the Autism Diagnostic Observation Schedule, a non-parametric Kruskall- Wallis test was used. The analysis showed statistically significant differences on the mean ranks of the Autism Diagnostic Observation Schedule Total score and sub-domains between syndrome groups. Table 4.6.5 summarises the mean ranks raw scores and the statistical results of the analyses.

Table 4.6.5: Mean ranks and the statistical results on the Total scores, and sub-domains Scores of the ADOS for children with the isolated Hypopituitarism, Optic Nerve Hypoplasia and Septo Optic Dysplasia syndrome groups.

Autism Diagnostic Observation Schedule	Diagnosis	Mean Rank	Kruskall- Wallis χ^2 *df* *p-value*
Total Score	Hypopituitarism	15.46	14.79 2 .001**
	Optic Nerve Hypoplasia	27.61	
	Septo Optic Dysplasia	35.46	
Reciprocal Social Interaction	Hypopituitarism	15.50	14.82 2 .001**
	Optic Nerve Hypoplasia	27.43	
	Septo Optic Dysplasia	35.54	
Communication	Hypopituitarism	19.57	8.12 2 .02*
	Optic Nerve Hypoplasia	27.07	
	Septo Optic Dysplasia	33.68	

***Conferring correction at $p < 0.017$;*Higher mean rank scores indicate greater ASD tendencies*

As the Kruskall -Wallis test does not employ post- hoc analysis to investigate where statistical significances are positioned between participant group memberships, children with Hypopituitarism, Optic Nerve Hypoplasia and Septo Optic Dysplasia were compared using between groups pair-wise comparisons. A comparison between children with Optic Nerve Hypoplasia and isolated Hypopituitarism mean rank score, revealed no significant statistical differences between the Autism Diagnostic Observation Schedule, Total score, (U (28) = 59.50, $p > 0.05$) Social Interaction sub-

domain, (U (28) = 61.50, $p > 0.05$) and the Communication sub-domain scores (U (28) = 71.00, $p > 0.05$).

Secondly, a comparison of mean rank scores between children with isolated Hypopituitarism and Septo Optic Dysplasia revealed significant statistical differences between the Autism Diagnostic Observation Schedule, Total score, (U (42) = 52.00, $p < 0.05$), Social Interaction sub-domain, (U (42) = 50.50, $p < 0.05$), and the Communication sub-domain scores (U (42) = 98.00, $p < 0.05$).

Comparisons between children with Septo Optic Dysplasia and Optic Nerve Hypoplasia revealed no significant statistical difference between the mean ranks of the Autism Diagnostic Observation Schedule, Total score (U = (42) =1.88, > 0.05), Social Interaction sub-domain (U = (42) =1.93, > 0.05), or the Communication sub-domain scores, (U = (42) =1.70, < 0.05).

The comparison of raw scores on the Social Communication Questionnaire Communication sub- domain between participant groups

Looking at the SCQ, to explore the statistical differences for the severity of autistic symptomology between syndrome groups, a non-parametric Kruskall- Wallis test was used. The analysis found statistically significant differences on the mean ranks of the Social Communication Questionnaires Total score, and the Social Interaction and communication sub-domain, between syndrome groups, and these finding are summarised in table 4.6.6.

Table 4.6.6: The mean ranks and the statistical results on the Total score, Reciprocal Social Interaction and Communication domain of the SCQ for children with isolated Hypopituitarism, ONH and SOD syndrome group

Social Communication Questionnaire	Diagnosis	Mean Rank	Kruskall- Wallis χ^2	*df*	*p* value
Total Score	Hypopituitarism	13.86			
	Optic Nerve Hypoplasia	30.43	15.80	2	.00 **
	Septo Optic Dysplasia	35.86*			
Social Interaction	Hypopituitarism	16.43			
	Optic Nerve Hypoplasia	28.82	11.47	2	.00 **
	Septo Optic Dysplasia	34.38*			
Communication	Hypopituitarism	14.18			
	Optic Nerve Hypoplasia	29.29	15.88	2	.00**
	Septo Optic Dysplasia	35.27*			

***Bonferroni correction at $p < 0.017$; *Higher mean rank scores indicate greater ASD tendencies*

To investigate where statistical significance was positioned between child group membership, children with isolated Hypopituitarism, Optic Nerve Hypoplasia and Septo Optic Dysplasia were compared using pair-wise comparisons between groups. A comparison between children with Optic Nerve Hypoplasia and isolated Hypopituitarism, showed statistically significant differences between the SCQ Total score, (U (28) = 30.50, $p < 0.05$), the SCQ Social Interaction domain, (U (28) = 52.00, $p < 0.05$), and the SCQ Communication domain, (U (28) = 35.00, $p < 0.05$). Secondly, comparisons between children with isolated Hypopituitarism and Septo Optic Dysplasia found statistically significant differences between the SCQ Total score, (U (42) = 58.00,

$p < 0.05$), SCQ Social Interaction domain, (U (42) = 73.00, $p < 0.05$), and the SCQ Communication domain (U (42) = 58.50, $p > 0.05$).

Lastly, comparison between children with Septo Optic Dysplasia and Optic Nerve Hypoplasia revealed no statistically significant differences between the mean ranks of the SCQ total score (U = (42) =155.50, > 0.05), the Social Interaction sub-domain (U = (42) =154.50, > 0.05), or the SCQ Communication sub- domain, (U = (42) = 144.00, > 0.05).

The relationship and differences between Intellectual Disability, Visual Acuity and Autistic Spectrum Disorders.

As no children with isolated Hypopituitarism scored above the cut-off point for autistic disorders according to the ADOS, SCQ or Clinician Diagnosis, the following sections will explore the relationship between intellectual ability and visual acuity in children with Septo Optic Dysplasia and Optic Nerve Hypoplasia only.

The relationship between visual impairments and autistic phenomenology

To assess for differences between children's level of visual function and autistic symptomology, children's level of visual function (e.g. impaired, severe and profound) was used as a grouping variable, rather than participant group.

Although, no statistical associations were reported between children's levels of visual acuity and scoring above, or below the cut-off point for Autistic Spectrum Disorders, on the Autism Observation Schedule, or receiving a diagnosis of autism from a Clinician, statistically significant associations were reported between scoring above

the cut-off point for Autistic Spectrum Disorders on the Social Communication Questionnaire. The Chi-squared statistical test of association is summarised in table 4.6.7.

Table 4.6.7: The number of children scoring above the suggested cut-off point for Autistic Spectrum Disorders on the SCQ, ADOS and Clinician diagnosis.

Level of visual acuity	SCQ		ADOS		Clinician	
	-	+	-	+	-	+
Impaired (n=16)	10	6	10	6	12	4
Severe (n=12)	7	5	7	5	9	3
Profound (n =14)	1	13	6	8	7	7
Chi Square	$\chi^2 = 10.99; 2; < 0.01$*		$\chi^2 = 1.25; 2; > .01$		$\chi^2 = 1.56; 2; > .01$	

* + = *above cut-off point*, - = *below cut-off point for Autistic Spectrum Disorders on the ADOS, SCQ and Clinician Diagnosis.*

The relationship between degree of intellectual disability and Autistic Phenomenology

Using the degree of intellectual disability (e.g. above/average, mild, moderate, and severe/ profound) as a grouping variable, rather than visual acuity, the number of children scoring above the suggested cut-off point for Autistic Spectrum Disorders on the Autism Diagnostic Observation Schedule, the Social Communication Questionnaire and receiving Clinician diagnosis of autism was compared. Statistical association was found between the degree of intellectual disability, and scoring above or below the cut-off point for Autistic Spectrum Disorders, on the Autism Observation Schedule and Social Communication Questionnaire, but not on receiving a diagnosis of autism from a Clinician, table 4.6.8. summarises these findings.

Table 4.6.8: The percentage of children scoring above the suggested cut-off point for ASD, and statistical analysis on the SCQ, ADOS and Clinician diagnosis according to degree of Intellectual Disability for children with SOD and ONH.

Degree of Disability	SCQ		ADOS		Clinician	
	-	+	-	+	-	+
Above/Average (n=12)	10	2	11	1	11	1
Mild (n=9)	4	5	5	4	6	3
Moderate (n=13)	3	10	4	9	7	5
Severe/Profound (n=8)	1	7	3	3	4	4
Chi - Square	χ^2 = 13.12; 3, < 0.01*		χ^2 = 10.58; 3, < 0.01*		χ^2 = 5.34; 3, >0 .01	

** Statistical significance achieved at 0.01, + = above cut-off point, - = below cut-off point for Autistic Spectrum Disorders on the ADOS, SCQ and Clinician Diagnosis.*

Statistically significant differences were also found between the classification of intellectual disability, and the Total and domain raw score of the Autism Diagnostic Observation Schedule. However, only the domain of Social Interaction, of the Social Communication Questionnaire reported statistically significant differences. Table 4.6.9 summarises these findings.

Table 4.6.9: Mean ranks and the statistical results on the total score, Reciprocal Social Interaction and Communication domain of the SCQ and ADOS for children with ONH and SOD according to degree of Intellectual Disability.

	Degree of Disability	Mean Rank	χ^2	*df*	*p-value*
Social Communication Questionnaire					
SCQ Total	Above/Average	11.88			
	Mild	18.72			
	Moderate	28.50	14.15	3	.01**
	Severe/Profound	27.69			
Social interaction	Above/Average	11.13			
	Mild	17.39			
	Moderate	29.62	18.02	3	.00**
	Severe/Profound	28.50			
Communication	Above/Average	13.67			
	Mild	18.61			
	Moderate	24.42	10.80	3	.01**
	Severe/Profound	30.13			
Autism Diagnostic Observation Schedule					
ADOS Total	Above/Average	13.71			
	Mild	16.94			
	Moderate	25.81	10.59	3	.02
	Severe/Profound	28.19			
Communication	Above/Average	13.17			
	Mild	16.81			
	Moderate	26.88	12.37	3	.02
	Severe/Profound	27.38			
Reciprocal Interaction	Above/Average	13.88			
	Mild	17.50			
	Moderate	25.96	14.15	3	.01**
	Severe/Profound	27.13			

***Bonferroni correction at 0.017*

The relationship between Intellectual Disability and Autism Phenomenology in children with ONH/SOD with the removal of children with profound intellectual disability.

Four children were removed from the subsequent analysis due to their level of profound intellectual disability. Even so, significantly statistical associations were still reported for scoring above the cut-off point for autistic disorders and children's level of visual acuity, on the SCQ, but not on the ADOS or receiving a diagnosis of autism from a Clinician. Table 4.6.9.1 summarises these findings.

Table 4.6.9.1: The number of children scoring above the suggested cut-off point for Autistic Spectrum Disorders on the SCQ, ADOS and Clinician diagnosis

Level of visual acuity	SCQ		ADOS		Clinician	
	-	+	-	+	-	+
Impaired (n=16)	10	6	10	6	12	4
Severe (n=11)	7	4	7	4	8	3
Profound (n=11)	1	10	5	6	6	5
Chi Square	χ^2 = 9.10; 2, < 0.01*		χ^2 = 0.99; 2, > .01		χ^2 = 1.41; 2, > .01	

Statistically significant associations were still found between the degree of intellectual disability, and scoring above or below the cut-off point for Autistic Spectrum Disorders on the ADOS and SCQ, but not on receiving a diagnosis from a Clinician, even with the removal of the four children with profound intellectual disability. Table 4.6.9.2 summarises these findings.

Table 4.6.9.2: number of children scoring above the suggested cut-off point for Autistic Spectrum Disorders on the SCQ, ADOS and Clinician diagnosis showed no significant differences according to degree of intellectual disability.

Degree of Intellectual Disability	SCQ		ADOS		Clinician	
	-	+	-	+	-	+
Above/Average(n= 12)	10	2	11	1	11	1
Mild (n= 9)	9	5	5	4	6	3
Moderate (n=10)	3	7	4	6	6	4
Severe (n=7)	1	6	2	5	3	4
Chi- Square	χ^2 = 10.54; 2, < 0.01*		χ^2 = 9.42; 2, < 0.01*		χ^2 = 5.46; 2, >0 .01	

From the analyses so far, it is not known whether the level of intellectual disability or visual loss has the greatest impact on autistic phenomenology in children with Septo Optic Dysplasia and Optic Nerve Hypoplasia, and to assess this, a binary logistic regression was used.

The categorical dependent variable was scoring above the cut-off point for Autistic Spectrum Disorders on the Social Communication Questionnaire. A maximum of three independent predictors were entered due to the low number of children, and children with isolated Hypopituitarism were included to increase the numbers. The two continuous independent variables were: the mean-age equivalence scores of the Adaptive Behaviour Composite to assess degree of intellectual disability and Expressive Language mean-age equivalence, both from the Vineland Adaptive Behaviour Scales. The third categorical variable was degree of visual impairment.

The best predictor of scoring above the cut- off point for Autistic Spectrum Disorders on the Social Communication Questionnaire was level of visual acuity but only marginally, yielding a R^2 of .53. Severity of language impairment did not predict classification of Autistic Spectrum Disorders. However, degree of intellectual disability did add to the model significantly. Table 4.6.9.3 summarises these findings.

Table 4.6.9.3: Binary logistic Regression of Autistic Spectrum Disorders and its possible predictor variables in children with SOD and ONH

Variable	Standardised B	*T*	*P*
Level of Vision	-2.895	56.247	.000
Intellectual Disability	-.047	51.986	.000
Expressive language	-.008	6.263	ns

4.7 Discussion

The present study is the first to have systematically assessed the prevalence of autistic phenomenology in children with Septo Optic Dysplasia, Optic Nerve Hypoplasia and isolated Hypopituitarism. It was anticipated that by using these three closely related clinical conditions that this could help to identify whether hormonal loss, visual loss, or intellectual disability better accounted for autistic phenomenology in the present cohort of children. At the same time, the study also recognised that, with the absence of a standardised tool for the measurement of autistic disorders in children with

visual loss, it was critical that the psychometric properties of the adapted Autism Diagnostic Observation Schedule created in Chapter Three were investigated further.

The evaluation of the psychometric properties of the measures used to assess and identify Autism Spectrum Disorders

Overall, good levels of validity were achieved from Clinician diagnosis, the Autism Diagnostic Observation Schedule and the Social Communication Questionnaire, but not the Gilliam Autism Rating Scale.

The Pearson rank correlation coefficients revealed that the Autism Diagnostic Observation Schedule and the Social Communication Questionnaire were significantly correlated on Total Score levels and the sub-domain level of Social Interaction. Moderate correlations were reported between the sub domains of Communication. For these two assessments. This endorses the use of both of these measures in conjunction to investigate autistic disorders in children and visual loss. This supports Coresello *et al.*, (2007) recommendations that the Social Communication Questionnaire and the Autism Diagnostic Observation Schedule are very effective when used in combination, but this combination is not as specific as the Autism Diagnostic Interview and Autism Diagnostic Observation Schedule. However, as both of these assessments can be time consuming for families the Social Communication Questionnaire and the Autism Diagnostic Observation Schedule are usually used more commonly for research purposes.

The concurrent validity between the Autism Diagnostic Observation Schedule and the Social Communication Questionnaire was good, although 26% of participants

who reached the cut-off point for Autistic Spectrum Disorders on the Social Communication Questionnaire did not reach the cut-off point for autism on the Autism Diagnostic Observation Schedule. Even though good agreement levels were also achieved between Clinician diagnosis and the Autism Diagnostic Observation Schedule, 36% of those who met the cut–off point for Autism Spectrum Disorders on the Autism Diagnostic Observation Schedule, did not receive a diagnosis of Autism from a Clinician. In support of these findings, previous research by Howlin and Karp (2002) reported similar agreement levels between the Social Communication Questionnaire and Autism Diagnostic Observation Schedule.

Surprisingly, agreement between the Social Communication Questionnaire and Clinician Diagnosis was only moderate (Kappa = 0.46). This result can be attributed to the questionnaire being a screening instrument rather than a diagnostic tool and that parents completed the questionnaire rather than a trained Clinician. The finding also supports that utilisation of the Social Communication Questionnaire as an appropriate tool to screen for Autistic disorders in combination with Clinician Diagnosis and/or the Autism Diagnostic Observation Schedule in the present cohort of children. In further support the Receiver Operator Curve corroborated these findings, with the Autism Diagnostic Observation Schedule and the Social Communication Questionnaire both reaching good sensitivity and specificity levels against a diagnosis of autism from a Clinician.

Overall, the Gilliam Autism Rating Scale reported poor discriminative properties in the present study. Cohen's Kappa agreement values between the Autism Diagnostic Observation Schedule and the Gilliam Autism Rating Scale were reported as

only moderate (Kappa = 0.44) and agreement between Clinician diagnosis and the Gilliam Autism Rating Scale was 0.39. This result is in line with recent studies which have reported that the Gilliam Autism Rating Scale may miss as many as 58% of children with Autistic Disorder (Lecavalier, 2005; South *et al.,* 2002). The present study also demonstrates the strength of using comprehensive observational techniques such as Clinical diagnosis or the Autism Diagnostic Observation Schedule for the diagnosis of autism in children who present with complex clinical pictures. South *et al.*, (2002) also reported that the phrasing of questions in the Gilliam Autism Rating Scale often left parents confused, and this could have contributed to the scale's poor psychometric properties. South *et al.*, (2002), do acknowledge that the Gilliam Autism Rating Scale has not received as much research attention as other autism assessments, however research which has been published has only reported modest psychometric data in comparison to the strong psychometric properties reported by Gilliam (1995).

The current cohort of children included children with profound disabilities and high functioning adolescents. Therefore, the levels of associated intellectual disability in children need to be considered when interpreting autistic phenomenology in children with Optic Nerve Hypoplasia and Septo Optic Dysplasia. Gray, Bruce, Tonge and Sweeney (2007), state that caution is needed when interpreting autistic behaviours in children with low developmental ages. Furthermore, Lord and Risi (1998) found that diagnostic tools lost their specificity when used with children with profound learning disabilities and with high functioning adults.

The further complex issue of visual loss in children also needs to be addressed, but to date no research has examined the psychometric properties of instruments used to

diagnose autism within a blind population, which makes this extremely difficult. For these reasons, the results of the present study cannot be compared to previous research which considers the impact of both visual impairments and intellectual disability.

Importantly, the present study demonstrated that autistic phenomenology can be measured, and identified in children with Septo Optic Dysplasia and Optic Nerve Hypoplasia, when the appropriate adaptations or exclusions are made to the materials and scoring criteria of instruments used to diagnose autism.

The systematic assessment of Autistic Spectrum Disorders in the current population of children with Septo-Optic Dysplasia, Optic Nerve Hypoplasia and isolated Hypopituitarism.

This is the first study to have systematically assessed Autistic Spectrum Disorders in the current population of children with Septo Optic Dysplasia, Optic Nerve Hypoplasia and isolated Hypopituitarism. Comparisons between children with isolated Hypopituitarism, Optic Nerve Hypoplasia and Septo Optic Dysplasia indicated that children with isolated Hypopituitarism did not meet the cut off point for Autistic Spectrum Disorders, demonstrating that hormone deficiencies alone did not make children vulnerable to autistic behaviours. This suggests that the group characteristics, of visual loss, and intellectual disability in children with Septo Optic Dysplasia and Optic Nerve Hypoplasia accounted for their autistic phenomenology.

To support the relationship between intellectual disability and autism in children with Septo Optic Dysplasia and Optic Nerve Hypoplasia an increased number of children were categorised with Autistic Spectrum Disorders on module One and module

Two, of the Autism Diagnostic Observation Schedule, which were both used for children with no speech or simple phrase speech. This indicated that the results of the study could be explained by the characteristics of intellectual disability in lower functioning children. However, many of these children also had accompanying levels of visual impairments, which made it difficult to disentangle the impact of visual loss from that of intellectual disability when explaining autistic behaviours.

In further support, statistically significant differences were also found between the degree of intellectual disability, and scoring above, or below the cut-off point for Autistic Spectrum Disorders on the Septo Optic Dysplasia and Optic Nerve Hypoplasia, but not on receiving a diagnosis from a Clinician, and this persisted, even with the removal of the four children with profound intellectual disability. In addition, the removal of children with profound intellectual disability still produced the same results, which further endorsed the relationship between intellectual disability and autism in children with Septo Optic Dysplasia and Optic Nerve Hypoplasia.

Thirteen of the fourteen children with profound visual loss were indicated as having of autistic disorders according to the Social Communication Questionnaire. When the Autism Diagnostic Observation Schedule was used, this reduced to eight children, and Clinician diagnosis further reduced the number to seven children. Therefore, parents tended to over report autistic tendencies in children who had profound visual loss, in comparison, to children with impaired or severe visual impairments. In addition, statistically, no differences were reported between scoring above or below the cut-off point for autism and the degree of visual loss according to the Autism Diagnostic Observation Schedule and Clinician diagnosis, unlike the Social

Communication Questionnaire. These results indicate that detailed Clinical assessment, or the use of the Autism Diagnostic Observation Schedule, may reduce the possibility of a false positive diagnostic classification overshadowing children with visual loss.

At raw domain and total level scores of the Septo Optic Dysplasia and Optic Nerve Hypoplasia, the difference between the severity of autistic behaviours and visual acuity, found no statistically significant findings. However, statistically significant differences were found between intellectual disability, and the Total, Social Interaction and Communication domain of the Autism Diagnostic Observation Schedule, but not on the domain of Social Interaction of the Social Communication Questionnaire. This suggests that intellectual disability better accounted for the severity of autistic phenomenology in children with Septo Optic Dysplasia and Septo Optic Dysplasia, but also may have accounted for the reported differential reporting between the scales. However, the results from the binary regression revealed that Autistic Spectrum Disorders were predicated more strongly by intellectual disability than visual loss, but this finding was only marginal.

The findings of the present study are in line with early research by Chess (1971) who reported that the degree of intellectual disability was related to autistic behaviours in the blind and Ek *et al.,* (1999) who attributed neurological brain damage in children with ROP as the source of autistic behaviours and not visual loss. Most recently, When Parr *et al.*, (2008) factored out vision in children with Septo Optic Dysplasia and Optic Nerve Hypoplasia, developmental delays still persisted. Unfortunately, as the statistical analyses in this study was largely non-parametric this prevented the factoring out of vision, which could have identified whether intellectual disability or visual loss better

accounted for autistic disorders in the present cohort of children. Even if this was possible it would not have been possible to isolate the origin of developmental delays as reported by the Vineland Adaptive Behaviour Scale as being either due to their neurological impairments and/or visual loss.

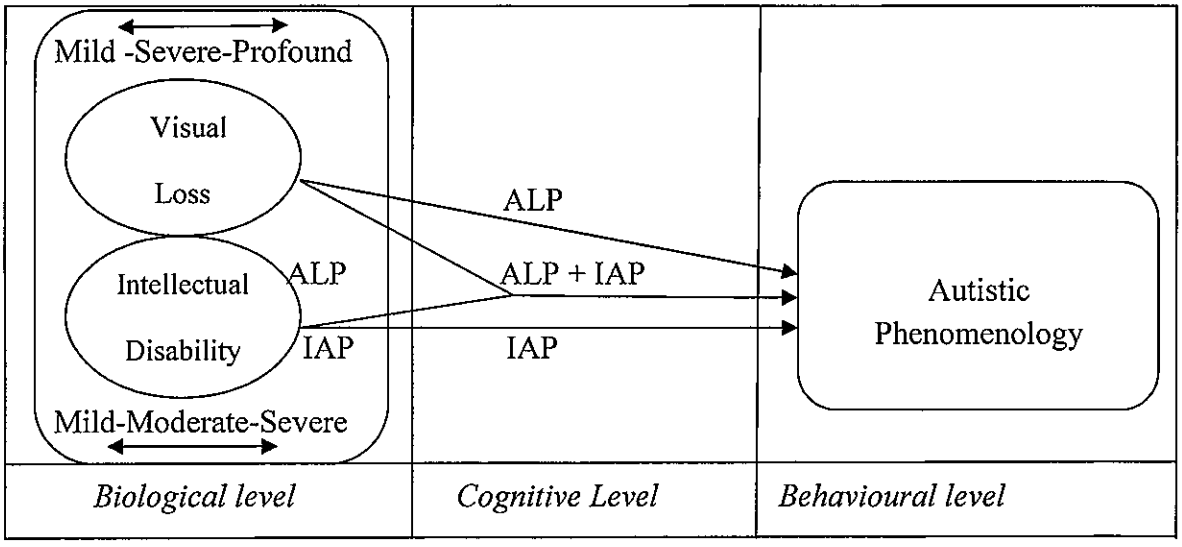
In a large scale study, Mukaddes *et al.*, (2007) reported that the autistic behaviours of 257 blind children and adults were largely due to both greater degrees of intellectual disability and greater severity of visual loss. This suggests that rather than determining that autistic behaviours are either due to visual loss or due to intellectual disability, the research by Mukaddes *et al.*, 2007 suggests that vulnerability to autistic phenomenology can be considered to occur on a spectrum of severity of clinical impairments.

The study by Parr *et al.*, (2008) reported the percentage of Autistic Spectrum Disorders in children with Septo Optic Dysplasia and Optic Nerve Hypoplasia as 22%, in comparison to the present study, the Social Communication Questionnaire reported 44%, the Autistic Diagnostic Observation Schedule 32%, the Gilliam Autistic Rating Scale 25%, and Clinician Diagnosis was 20%. These differences can be attributed to the differences in the methodology used, specifically the utilisation of parental, researcher or Clinician assessment of autism. Notably, similar percentages of autistic disorders were reported by Parr *et al.*, (2008) in their study, and Clinician diagnosis in the present study.

On a theoretical level, Brambring (2008) proposed that there were different processes for autism in sighted children, compared to that of children who were blind. Brambring (2008) considered that autism in sighted children was a result of a

pathological information processing impairment, whereas, blind autistic children encountered problems in information gathering, but only a few problems in information processing. However, what the present study also postulates is that impairments in information gathering and information processing may be interrelated and acting in tandem as a third pathway to autism.

Both these observations and previous research, it is likely that autism in children with Septo Optic Dysplasia and Optic Nerve Hypoplasia could be explained by three possible pathways. The Frith, Leslie and Morton (1991) causal model of autism has been adapted to explain the findings of the present study. Figure Eight shows that visual loss and intellectual disability were both contributing factors and possibly interrelated factors, in the occurrence of autistic phenomenology in children with Septo-Optic Dysplasia and Optic Nerve Hypoplasia.



**ALP = Autistic Like Pathway, IAP + Idiopathic Autistic Pathway*

Figure Eight: the three pathways to autistic phenomenology in children with Septo Optic Dysplasia and Optic Nerve Hypoplasia.

What is not known, is whether these three cognitive pathways account for differences of expressed autistic phenomenology at the behavioural level, or whether these three pathways converge at the cognitive level, and only produce one common pathway to autistic disorders and that differences in autistic phenomenology are accounted for by the severity of neurological impairments, or even external factors. Such external factors may include environmental provisions for the child, the age of diagnosis, and early intervention educational programmes. Furthermore, autistic like behaviours in the blind may be cognitively, and functionally adaptive for a blind child, but maladaptive for sighted autistic child.

Limitations of the present thesis

The present study demonstrates that, regardless of the pathway which accounts for autistic phenomenology in children with Septo Optic Dysplasia and Optic Nerve Hypoplasia, these children still require the appropriate educational provisions and early diagnosis of autism. In turn, this may help to differentiate between the transient autistic like behaviours from that of the persistent Kanner (1943) type autism which is often observed in sighted autistic children. However, it is not possible to differentiate between autism and autistic like behaviours until a standardised diagnostic instrument to assess autism in the blind is established. The difficulties of creating such an instrument lie in the low incidence of visual impairments, the heterogeneity of visual loss, its co-morbidity with intellectual disability, and more importantly trying to find a cohort of children on whom to standardise an assessment.

A methodological limitation was that diagnosis of visual loss was not received by an ophthalmologist and relied on parental reporting for the severity of visual loss. This prevented the detailed assessment of the relationship of visual loss and autistic disorders. This limitation occurred due to the medical records at the Birmingham Children's Hospital not containing detailed data about children's vision. In addition, Due to the low incidence rate of the clinical conditions three charities were also approached for the thesis, this lead to the absence of detailed medical records to shed light on children's complete clinical picture. It was considered that parental reporting for the degree of visual loss would be most accurate in the absence of this vital information. In fact, the diagnosis of Optic Nerve Hypoplasia and Septo Optic Dysplasia for children from charities could also not be corroborated through medical records, and this could have resulted in inaccurate clinical group membership. As these two clinical conditions are closely related, further medical testing through the lifespan of the child could mean that clinical diagnosis of these two conditions could have changed over time.

Future suggestions for follow up research

Future research will need to explore how children acquire information about their social and communicative world from their intact senses compared to how they process this information. and this can be achieved through cognitive neuroscience techniques. The developmental trajectories of children with visual loss and/or autism needs to be closely examined through longitudinal research methodologies to establish when these children reach certain developmental milestones and are at risk from

specific psychosocial factors. Longitudinal research can also assess whether autistic behaviours in the blind are only surface similarities and transient features (Baron-Cohen, 2002) by following children who have been identified as having autistic disorders in the present cohort and assessing their autistic behaviours over a period of time. Importantly, when explaining autistic symptoms in the visually impaired, the early developmental profiles and, current levels of intellectual disability and associated impairments need to be carefully observed.

Implications and summary of the present study

Early identification enables the children to access appropriate early intervention services (South *et al.*, 2003). Research has shown that early involvement in intervention programmes is positively correlated with improvements in functioning and a reduction in symptomatology (Howlin, 1997). Educational provisions will need to be tailored to account for children's visual loss and intellectual disability, but presently there is no national educational strategy for children who present with these two disorders.

From the findings of the present thesis it is recommended that diagnosis of autism in children with visual loss should include Clinician diagnosis, the adapted Autism Diagnostic Observation Schedule, the Social Communication Questionnaire and the incorporation of children's full developmental histories. This ensures that for best practice, Clinicians are provided with a complete clinical picture of the child, which has been sourced from a multidisciplinary team of professionals.

CHAPTER FIVE

THE ADAPTIVE AND COGNITIVE PROFILES OF CHILDREN WITH SEPTO OPTIC DYSPLASIA, OPTIC NERVE HYPOPLASIA AND ISOLATED HYPOPITUITARISM

5.1 Background to Chapter Five

The empirical component of Chapter Four reported that Autistic Spectrum Disorders were a frequent occurrence in children with Septo-Optic Dysplasia and Optic-Nerve Hypoplasia, but not in children with isolated cases of Hypopituitarism. This indicated that children's level of intellectual disability and their degree of visual loss, rather than hormonal loss, were significant causative factors of autistic phenomenology in this cohort of children. Chapter Four, also reported the first systematic investigation of the differential reporting of Autistic Spectrum Disorders between four different screening and diagnostic assessments in children with Septo-Optic Dysplasia and Optic-Nerve Hypoplasia.

The findings of Chapter Four can be explained by the complex child characteristics that children presented in the present clinical cohort. It is possible that the varying severities of visual loss and/or intellectual disability made it difficult to disentangle autistic phenomenology from that of intellectual disability, or visual loss in children with Septo Optic Dysplasia and Optic Nerve Hypoplasia. This uncertainty may have contributed to the over representation of autistic disorders in Chapter Four, and the reported differential diagnosis of autistic phenomenology amongst the screening and diagnostic tools. For these reasons, it is important to seek a full developmental profile

of children who present with intellectual disability and/or visual loss to aid accurate diagnosis of Autistic Spectrum Disorders.

Previous research has reported the high co morbidity of intellectual disability and visual loss, and therefore it is important to seek the full developmental profiles of children who present with such clinical profiles. It has been reported that greater severities of visual impairment are usually directly proportional to greater levels of intellectual disability (Warburg, 2001). It is also estimated that at least 25% to 63% of individuals with a visual impairment, also have some form of intellectual disability (Janicki, & Dalton, 1998; Lavis, 1994). Knowing that intellectual disability is a contributing factor to autistic phenomenology, and a characteristic of the syndromes, Septo Optic Dysplasia and Optic Nerve Hypoplasia, research has yet to fully assess the impact of this characteristic upon autistic disorders.

With the further complexity of visual loss, it is not fully understood how this symptomatology interacts with, and impacts the cognitive development of children with Septo Optic Dysplasia and Optic Nerve Hypoplasia. Consequently, difficulties exist when researchers attempt to disentangle these symptomologies from one another. This task is further complicated by the scarcity of available research that maps the developmental profiles of children with Septo Optic Dysplasia and Optic Nerve Dysplasia, and for such reasons, it becomes increasingly difficult to present a complete clinical picture of children with these two syndromes and/or Autistic Spectrum Disorders.

5.2 Overview of Chapter Five

To ensure best practice for the diagnosis of autism, Howlin (2000) recommends that an individual who is suspected of having an autistic disorder must have their cognitive profiles, receptive language skills, expressive language skills, and developmental histories investigated thoroughly, and this is typically completed by the use of standardised assessment tools by qualified professionals. Based on these recommendations, Chapter Five will aim to examine the profile of intellectual disability in children with Septo-Optic Dysplasia and Optic-Nerve Hypoplasia by investigating children's adaptive and cognitive profiles. To address the lack of research available on the cognitive and adaptive profiles of children with visual loss and intellectual disability, Chapter Five will review literature which has reported the common co-occurrence of intellectual disabilities in children with autistic disorders (La Malfa *et al.*, 2004; Wing, 1979), genetic disorders and visual impairments.

Secondly, the literature review will examine research which investigates the relationship between the cognitive and adaptive profiles of children with different clinical aetiologies. Lastly, the empirical component of the thesis will aim to use a fine grained approach to the analysis of adaptive behaviours of children in the present thesis. This will include an examination of the domains and sub-domains of Vineland Adaptive Behaviour Scale. It is anticipated that this will help to identify whether children within the cohort show a distinctive adaptive behavioural profile. In addition, the relationship between cognition, adaptive behaviours and Autistic Spectrum Disorders will be examined. The findings of this analysis will be compared to previous research in order

to establish whether children with Septo Optic Dysplasia and Optic Nerve Hypoplasia and autistic disorders show similar profiles to that of previous research within this area.

5.3 Introduction to literature review

A diagnosis of intellectual disability is made when a child demonstrates three of the two criteria stipulated by the DSM-IV-TR (APA, 2000); (1) an intelligence quotient below seventy, (2) significant impairments in two or more areas of adaptive functioning (communication, self-care, home living, social/interpersonal skills, use of community resources, self-direction, functional academic skills, work, leisure, health, and safety), and (3) these impairments must be present before the age of eighteen.

The DSM-IV-TR (APA, 2000) describes the severities of intellectual disability through Intelligence Quotients (IQ). Intelligence Quotients describe measures of cognitive abilities of individuals in relation to their age group. A Mild deficit is defined as an Intelligence Quotient level of 50-55 to approximately 70; a moderate deficit is an Intelligence Quotient level of 35-40 to 50-55, a Severe deficit is an Intelligence Quotient level of 20-25 to 35-40, and a Profound deficit is an Intelligence Quotient level below 20 to 25.

Intelligence Quotients are derived through the use of standardized intelligence tests. Among the vast selection of intelligence tests for children, the Wechsler Intelligence Scale for Children-III (WISC-IIII; Wechsler, 2004) is the current "gold standard". The test comprises of a number of different Verbal subtests, which measure areas such as, vocabulary knowledge, general information about the world, verbal abstract reasoning, social judgment and common sense, arithmetic skills, short-term

memory and attention. The Performance subtests measure nonverbal areas including visual-motor coordination, perceptual organization, visual abstract reasoning, and attention to detail.

Klassen, Neufeld, and Munro (2005) recommend that an intelligence measure alone is not necessarily an indication of an intellectual disability. An assessment of a child's adaptive behaviour, by a standardised assessment tool is typically required when making a diagnosis of intellectual disability in children. Conceptually, adaptive behaviours describe both developmental and social constructs, these govern the way an individual interacts, and responds to demands placed upon them by their social and physical world (Dykens, Hodapp & Leckman, 1994).

A number of different assessments exist for the assessment of adaptive behaviours, and the format of these is usually a semi-structured interview given to the primary caregivers by a qualified clinician. The Adaptive Behaviour Assessment System-Second Edition (ABAS-II; Harrison & Oakland, 2003) is a commonly used instrument that measures adaptive behaviour and related skills. In addition, the Scales of Independent Behavior-Revised (SIB-R; Bruininks, Woodcock, Weatherman, & Hill, 1997) is another comprehensive measure of adaptive and problem behaviours. Currently the most frequently used assessment by professionals is the Vineland Adaptive Behaviour Scale (VABS; Sparrow, Balla & Cicchetti, 1984) and it measures the areas of Socialisation, Daily Living Skills, and Communication. The Vineland Adaptive Behaviour Scale has been used across a wide range of syndromes, which include intellectual disability in their behavioural profiles. Specifically, Down's syndrome (Loveland & Tunali-Koroski, 1998; Rodrigue, Morgan, & Geffen, 1991),

Prader-Willi syndrome (Dykens, Hodapp, Walsh, & Nash, 1992) Costello syndrome (Axelra, Nicholson, Stabley, Sol-Church & Gripp, 2007), Cohen syndrome (Karpf, Howlin, & Turk, 2005) and Autistic Spectrum Disorders (Carpentieri & Morgan, 1996; Schatz & Hamdan-Allen, 1995; Volkmar *et al.*, 1987).

The Adaptive and Cognitive profiles of children and intellectual disability and autism

Autistic children's cognitive and adaptive abilities have been documented as significant predictors for the severity of their autistic symptomology, and for these reasons the evaluation of their adaptive functioning and cognitive ability is commonly required (Volkmar *et al.*, 1987). This evaluation aids in the diagnosis of Autistic Spectrum Disorders, and helps to reduce the occurrences of diagnostic overshadowing by Clinicians. Importantly, after diagnosis, the examination of a child's cognitive and adaptive profiles can help to identify areas of development that require specific educational and/or behavioural interventions (Gillham, Carter, Volkmar, & Sparrow, 2000; Filipek *et al.,* 1999).

Autism is reported at all intellectual levels, from high cognitive functioning levels to profound levels of impairments. Children with intellectual disabilities and/or Autistic Spectrum Disorders, tend to a have a distinctive behavioural profile. For example, children with autism and intellectual disability show greater impairments in the Social domains of the Vineland Adaptive Behaviour Scale, compared to children with only an intellectual disability, who demonstrate lower scores across all sub-domains (Burack & Volkmar, 1992; Volkmar *et al.*, 1987). More recently, adopting the micro analysis of scores on sub-domains of the Vineland Adaptive Behaviour Scale, has

shown that individuals with autism have tended to score highly in the Motor and Daily Living domains, and the lowest on the Socialization domain (Kraijer, 2000). During a large scale study, Carter *et al.*, (1998) examined the adaptive behaviour of 684 children and adults with autism. Even when groups were separated according to their age and language ability, they both demonstrated the expected "autism profile" of higher Daily Living Skills, lower Socialization scores, and intermediate Communication scores when age equivalent scores were used.

5.4 The assessment of adaptive and cognitive abilities in children with visual loss

According to Sattler (2002), visual experiences may influence the performance level of a child with congenital blindness in answering questions on cognitive tests. Knowing this, it was important to select a cognitive assessment that does not put children at a disadvantage due to their visual loss. The Wechsler Verbal Scale (Wechsler, 2004) is considered an acceptable intelligence test to use on populations of children with visual loss by clinicians. This test considered to give results which are comparable to those found for sighted children, even though there are certain items which may pose problems for a number of visually impaired children, and particularly those who are totally blind (Allan, 2002). For example, questions involving concrete concepts which are learned primarily through vision can be failed, whereas more difficult questions involving abstractions could be passed. In addition, subtests such as the "performance scale" include timing procedures which discriminate against those with low vision, as they allow the accruing of bonus points for rapid completion of

certain tasks and for these reasons, the subtest as a rule is always excluded when assessing children with visual loss (Warren, 1984).

The Wechsler scales have shown a tendency for children with visual impairments to obtain lower scores on the Comprehension, Similarities and Information sub-sets when compared to their sighted peers, which can be explained due to much of one's social learning occurring through visual experiences (Warren, 1984). Visually impaired children can demonstrate higher scores on digit span test due to auditory memory being highly proficient (considered to be a compensatory skill in the blind) (Smits & Mommers, 1976). Additionally, children with visual impairments demonstrate higher levels of echolalia or non meaningful speech which again affects their performance on the test (Bulla, 2002). The Stanford-Binet Intelligence Scales, Fifth Edition (Roid, 2004) can be used on children with low vision, as the only subtest that has a timing limit is the "analysis test", and the time limit is thought to be sufficient for visually impaired children. Some items, even on the verbal scales, have been shown to be biased against children who have profound or early (congenital or soon after) loss of vision (Warren, 1984).

The Slossen Intelligence Test (Slossen, 1963) has demonstrated strong psychometric properties when Hammill, Crandell and Colarusso (1970) used it on a heterogeneous group of thirty-two children with visual loss. More recently, the Slosson Intelligence Test-Revised (Slosson, Nicholson, & Hibpshman, 2002) now includes a supplementary manual for the visually impaired and the blind, which allows for the testing of cognition, with the removal of sub-sets. The investigation of intelligence testing in children with visual loss has received little attention in recent years, but as the

Slosson Intelligence Test-Revised includes the supplementary manual for children with visual loss, it was selected for use on all three groups of children.

Looking at the assessment of adaptive behaviours, a specific measure of for the visually impaired is the Reynell-Zinkin Scales: Developmental Scales for Young Visually Handicapped (Reynell, 1979), it measures Social Adaptation, Sensori-Motor Understanding, Exploration of Environment, Responses to Sound, Verbal Comprehension, Vocalization & Expressive Language (Structure), and Vocabulary Content of visually impaired children. The main advantage of the scale is that it includes domains unique to visually impaired children (i.e. exploration of environment and orientation and mobility skills). However, it is poorly standardised on only 109 visually impaired children, its criteria for "blind" and "visually impaired" is also questionable, as it includes twenty one children with multiple impairments, which lowers the ceilings values and results in inflated domain and overall scores (Warren, 1984). For the current research the scale was appropriate as it explores most areas of development, but it is no longer in print, and manuals could be located but no record sheets were available. For the present thesis, therefore the Vineland Adaptive Behaviour Scale was selected as a measure of adaptive behaviours as it has been previously used with individuals who have a visual impairment (Celeste, 2006; Kenworthy & Charnas, 1995) and it also includes a supplementary comparison group of blind children living in residential homes.

Summary of the aims of Chapter Five

Taking into consideration the importance emphasised by Clinicians and researchers, Chapter Five will addresses the impact of intellectual disability and

cognitive ability upon autistic phenomenology using standardised assessments which have previously been used in children with intellectual disability or visual loss.

Therefore, the aims of Chapter Five are too;

- Profile the Cognitive and Adaptive behaviours of children with Septo Optic Dysplasia and Optic Nerve Hypoplasia
- Investigate the relationship between the adaptive and cognitive profiles of children with Septo Optic Dysplasia and Optic Nerve Hypoplasia and their autistic phenomenology.

5.5 Methods

Participants

The removal of children with profound intellectual disability was also necessary when the cognitive and adaptive ability of children with Optic Nerve Hypoplasia were explored, as the selected intelligence test could not be use on children with mental ages below eighteen months. The Vineland Adaptive Behaviour Schedule identified children with profound intellectual disability through the classification of disability. After this removal from the cohort, this left nine children, of which four were female and five were male. The mean age in years was 8.02 years (SD: 36.86; age range 4.2-12.02 years). Two children were registered blind, and the remainder of children exhibited moderate to severe levels of visual impairment.

The group characteristics of children with isolated Hypopituitarism remained unchanged from that of Study Two and Study Three. The fourteen children in the group included four females and ten males, and the mean age of children was 11.10 years of

age (SD: 46.1; range: 5.2-16 years). Visual function was normal, and intellectual ability ranged from high to mildly low, and no children with Hypopituitarism were excluded when the cognitive and adaptive behaviours of these children were assessed.

Individual participant characteristics for each syndrome are presented in tables 5.5.1-5.5.3. Participant characteristics describe each child's chronological age, gender, level of visual loss (LP= light perception and AS = Astigmatism), Adaptive Behaviour Composite level and the reported presence (+) or absence (-) of Autism Spectrum Disorders according to the screening or diagnostic scales used to assess Autistic Spectrum Disorders.

Table 5.1: Child demographics for children with isolated cases of Hypopituitarism

Participant number	Diagnosis	Chronological Age (months)	Expressive Language (Months)	Gender	Vision	ABC Ability	ABC age equivalent (months)	SIT-R age equivalent (months)	SCQ
1	Hypopituitarism	146	186	Male	Normal	Adequate	119	57	-
2	Hypopituitarism	172	186	Female	Normal	Moderately Low	84	101	-
3	Hypopituitarism	160	42	Female	Normal	Mild	62	126	-
4	Hypopituitarism	109	135	Female	Normal	Adequate	101	86	-
5	Hypopituitarism	65	73	Male	Normal	Moderately High	94	101	-
6	Hypopituitarism	166	186	Male	Normal	Adequate	113	96	-
7	Hypopituitarism	170	186	Male	Normal	Adequate	86	75	-
8	Hypopituitarism	78	89	Male	Normal	Adequate	66	42	-
9	Hypopituitarism	79	186	Male	Normal	Adequate	113	62	-
10	Hypopituitarism	158	105	Male	Normal	Moderately Low	96	115	-
11	Hypopituitarism	192	186	Male	Normal	Mild	71	136	-
12	Hypopituitarism	192	186	Male	Normal	Adequate	104	55	-
13	Hypopituitarism	115	186	Female	Normal	Adequate	138	110	-
14	Hypopituitarism	72	105	Male	Normal	high	104	96	-

Table 5.2: Child demographics for children with Optic Nerve Hypoplasia (ONH)

Participant Number	Diagnosis	Chronological Age (months)	Expressive Language (months)	Gender	Vision	ABC Ability	ABC age equivalent (months)	SIT- R age equivalent (months)	SCQ
15	ONH	72	48	Male	Severe	Mild	54	68	-
18	ONH	125	105	Male	Profound	Moderate	164	99	+
19	ONH	36	51	Male	Impaired	Moderately High	15	27	-
21	ONH	80	186	Female	Impaired (AS)	Adequate	83	147	-
23	ONH	192	28	Male	Severe	Profound	89	24	+
24	ONH	70	186	Female	Impaired	High	71	104	-
25	ONH	102	186	Female	Impaired	High	103	108	-
26	ONH	110	105	Female	Impaired	High	196	125	-
27	ONH	112	105	Male	Impaired	Adequate	123	135	-
28	ONH	69	48	Female	Impaired	Adequate	105	68	-

Table 5.3: Child demographics for children with Septo Optic Dysplasia (SOD)

Participant Number	Diagnosis	Chronological Age (months)	Expressive Language (months)	Gender	Vision	ABC Ability	ABC age equivalent (months)	SIT- R age equivalent (months)	SCQ
28	SOD	50	78	Male	Profound	Mild	105	60	-
29	SOD	68	62	Male	Profound (LP)	Adequate	54	29	+
31	SOD	84	89	Male	Impaired	Adequate	92	75	-
33	SOD	108	78	Female	Impaired	High	172	84	+
35	SOD	120	135	Female	Severe (AS)	Mild	73	104	-
37	SOD	132	186	Female	Impaired	Mild	20	135	-
38	SOD	135	59	Male	Severe	Mild	86	80	+
40	SOD	149	105	Male	Profound (LP)	Mild Deficit	110	152	+
41	SOD	156	135	Male	Profound	Moderately Low	52	125	+
43	SOD	162	105	Male	Severe (AS)	Moderately Low	105	63	+
44	SOD	89	87	Female	Profound	Moderate	116	63	+
45	SOD	90	186	Female	Impaired	Moderate	63	99	-
46	SOD	106	53	Female	Profound	Moderate	13	60	-
47	SOD	108	190	Male	Severe	Moderate	101	98	-

48	SOD	101	20	Male	Profound	Moderate	41	113	-
50	SOD	192	105	Female	Profound	Moderate	68	63	+
51	SOD	141	105	Female	Impaired	Profound	110	92	+
52	SOD	61	45	Male	Profound	Severe	78	60	+
53	SOD	63	42	Male	Severe	Severe	147	80	-

Measures

Vineland Behaviour Scales (VABS; Sparrow, Balla, & Cicchetti, 1984)

The Vineland Adaptive Behaviours Scale examines the abilities of individuals from birth to the age of eighteen years. The Vineland Adaptive Behaviours Scale measures the four domains of Adaptive Behaviour: (1) the domain of Communication, with the sub-domains of Receptive, Expressive and Written Skills; (2) the domain of Daily Living Skills, with the further sub-domains of Personal, Domestic and Community; (3) the domain of Socialisation, which includes the sub-domains of Interpersonal Relationships, Play and Leisure and Coping Skills; and for children below the age of six years the Motor Skills domain which includes the sub domains of Fine and Gross Motor Skills. The raw scores from the three or four domains are converted into normative values. These standard scores are available for each behaviour domain and once added together make up the individual's Adaptive Behaviour Composite score (ABC) which gives a value to the global adaptive functioning derived.

Supplementary norms are further provided for the groups: ambulatory and non-ambulatory mentally retarded adults in residential facilities; ambulatory mentally retarded adults in residential facilities; non-ambulatory mentally retarded adults in residential facilities; mentally retarded adults in non-residential facilities; emotionally disturbed children in residential facilities; visually handicapped children in residential facilities and hearing impaired children in residential facilities. Within each sub-domain, the Vineland is divided into sets of items that probe a particular area of development. These sets each contain two to seven individual items. Each item within

the set is scored as a 0 (never), 1 (sometimes; partially), or 2 (usually), according to criteria detailed in the Vineland manual.

The Vineland Adaptive Behaviour Scale has reported good psychometric properties, with the Survey Form split half coefficients for the age groups under three ranging from 0.82 to 0.95 for the Domains and from 0.96 to 0.98 for the Adaptive Behaviour Composite. The Test-retest reliability for the Survey Form ranged from 0.78 to 0 .92 for the Domains, and 0.90 for the Adaptive Behaviour Composite. Inter-rater reliability for the Survey Form ranged from 0.62 to0 .78 for the Domains, and was 0.74 for the Adaptive Behaviour Composite.

The Internal consistency of the Survey Form, Split half means for Domains was 0.83 to 0.90 and for Adaptive Behaviour Composite it was 0.94. The Test – Retest mean of the Survey Form for Domains was reported as 0.81 to 0.86 and for Adaptive Behaviour Composite as 0.88 (N=484). Correlations between VABS and the Kaufman Assessment Battery for Children and the Peabody Picture Vocabulary Test-Revised, two intelligence tests, ranged from 0.07 to .52 and 0.12 to 0.37, respectively.

SIT-R3-1 Slosson Intelligence Test- Revised 3rd Ed (SIT-R3; Slosson, revised by: Nicholson & Hibpshman, 2002).

The newly revised edition of the Slosson Intelligence Test acts as a quick and reliable screening test of crystallized verbal intelligence. The supplementary manual for the visually impaired and the blind, allows the test to be used on all three groups of children in the present thesis. The SIT-R3 has minimal performance items and has

embossed materials allowing for testing of the visually impaired and the blind. It is one of the only measures of intelligence for these populations for both children and adults.

Cognitive areas of measurement include: 33 items on vocabulary 29, items about general information: 29 items about similarities and differences, 30 items about comprehension, 33 items concerning quantitative, and 34 items about auditory memory. A supplementary manual for the visually impaired and the blind is now included in the SIT-R3 manual. The supplementary manual includes embossed materials, and it is one of the only measures of intelligence for these populations for both children and adults.

Excellent Psychometric properties have been reported in the manual. The SIT-R 3 correlated 0.827 with the WISC-R, Verbal VIQ, even though the SIT-R3 does not cover Fluid performance. The Calibrated Norms reflect a high 0.828 correlation between the SIT-R3 TSS and the WISC-III Full Scale Intelligence Quotient. The Calibrated Norms Tables divide the Chronological Age every 3 months which is a refinement over earlier norms tables and re establish the 18+ ceiling level, applicable for adults through age 65 (Nicholson & Hibpshman, 2002).

It is designed for use by teachers, psychologists, guidance counsellors, special educators, learning disability instructors, and other responsible persons who often need to evaluate an individual's mental ability. The SIT-R3 is appropriate for U.S. and English speaking countries. Quantitative reasoning questions were designed to be administered to populations who use Metric or Standard references, using language common to both.

Social Communication Questionnaire (SCQ; Rutter, *et al.,* 2003)

In addition, the Social Communication Questionnaire was used to assess Autistic Spectrum Disorders. The total Social Communication Questionnaire score was used to assess the relationship between autistic disorders and adaptive behaviours and cognitive abilities in children.

Procedure

Data for the Vineland Adaptive Behaviour Scale (Sparrow *et al.*, 1984) was gathered during Study Three for all children. The Slossen Intelligence Test (Nicholson & Hibpshman, 2002) was administered to children before the Autism Diagnostic Observation Schedule (ADOS, Lord *et al*, 2001) and took from twenty to thirty minutes to complete. The SIT-R3 was administered in a quiet room with or without the presence of a teaching assistant or parent. Due to profound-severe intellectual disability not all children completed the Slossen Intelligence Test.

Data analysis strategy

For the purpose of comparability between the Vineland Adaptive Behaviour Scale (Sparrow *et al.*, 1984) and the Slossen Intelligence Test (Nicholson & Hibpshman, 2002), children with a profound disability who had completed the Vineland Adaptive Behaviour Scale were excluded for the analysis of intellectual disability as derived from the Adaptive Behaviour Composite of the Vineland Adaptive Behaviour Scale.

An exploratory analysis of data was initially conducted to establish whether the data met parametric assumption using the Shapiro–Wilks W tests of normality.

Furthermore, as recommended by Volkmar, (1987) age equivalent scores of each domain and sub-domain were used for statistical analysis of the Vineland Adaptive Behaviour Scale (Sparrow *et al*, 1984). Consistent with recommendations by Sattler (1988) and Silverstein (1986) Vineland age-equivalent as opposed to standard scores were used in the analyses.

The Adaptive Behaviour Mean Age Equivalence and the three domains of the Vineland Adaptive Behaviour Scale: Communication, Daily living Skills and Socialisation and the sub-domains of Play and Leisure and Coping Skills from the Daily Living skills domain were also normally distributed but violated homogeneity of variance assumptions. The sub-domains of Expressive Language and Receptive Language from the Communication domain, Personal, Domestic, Community from the Daily Living Skills Domain and Interpersonal Skills of the Socialisation domain were not normally distributed and also violated homogeneity of variance assumptions. Due to the unequal syndrome group sizes non-parametric tests were used when comparing children according to their syndrome group.

One way ANOVAs were used to assess the differences between children's level of vision and the Adaptive Behaviour Composite, the three domains, the sub domains mean age equivalence of the Vineland Adaptive Behaviour Scale and the SIT-R standard mean age scores. Children were split into four groups according to their level of visual acuity as (1) normal, (2) mild, (3) severe and (4) profound/blindness.

Pearson's correlation coefficients were used to assess the relationship between on the Adaptive Behaviour Composite standard, Domain and Sub Domain levels mean age equivalent scores of the Vineland Adaptive Behaviour Scales and mean age

equivalent score of the SIT-R3. T-tests were used to compare children who scored either above or below the cut off for Autistic Spectrum Disorders on the Social Communication Questionnaire.

5.6 Results

Differences between children with isolated Hypopituitarism, Septo Optic Dysplasia and Optic Nerve Hypoplasia on the Adaptive Functioning and domain levels of the Vineland Adaptive Behaviour Scale with Intellectual Disability Removed.

Table 5.6.1 shows that children differed significantly on the Domain levels of the VABS but not on the Adaptive Behaviour Composite of the VABS. The mean ranks and statistical analyses are summarised in Table 5.6.1.

Table 5.6.1: Mean ranks and statistical analysis of Mean Age Equivalence in Months on the Communication, Daily Living Skills and Socialisation Domains of the VABS for children with isolated Hypopituitarism, SOD and ONH

ABC composite and VABS Domain	Hypopituitarism (n=14)	Optic Nerve Hypoplasia (n=9)	Septo Optic Dysplasia (n=19)	Kruskall-Wallis Test		
	Mean age rank	Mean age rank	Mean age rank	χ^2	*df*	*p-value*
ABC	24.29	15.83	22.13	2.70	2	.260
Communication	28.25	20.06	17.21	6.69	2	.035*
Daily Living	29.18	19.22	16.92	8.45	2	015*
Socialisation	32.11	21.56	15.12	15.09	2	.001**

*** A Bonferroni correction to the alpha value was applied of 0.017 to avoid type I errors, * significance at 0.05*

Reported differences between children with isolated Hypopituitarism, Septo Optic Dysplasia and Optic Nerve Hypoplasia on the Sub- Domain levels of the Vineland Adaptive Behaviour Scale

Looking at the sub-domains of the Vineland Adaptive Behaviour Scales, children did not statistically differ between Expressive Language, Domestic skills or Coping Skills and syndrome group. Statistically significant differences were reported on the remainder of the sub domains of the VABS. Table 5.6.2 summarised the findings of this analysis.

Table 5.6.2: Mean ranks and statistical analysis of Mean Age Equivalence in Months of the Sub Domains of the Vineland Adaptive Behaviour Scale for children with isolated Hypopituitarism, SOD/ONH

VABS Sub Domain	Hypopituitarism (n=14)	ONH (n=9)	SOD (n=19)	Kruskall-Wallis Test		
	Mean Ranks			χ^2	*df*	*p-value*
Receptive Language	28.50	24.61	14.87	11.04	2	.004**
Expressive Language	27.07	20.33	17.95	4.75	2	.093
Written	29.21	20.67	16.21	9.19	2	.010*
Personal	29.79	17.94	17.08	9.64	2	.008*
Domestic	27.50	22.78	16.47	6.65	2	.360
Community	30.32	16.28	17.47	10.93	2	.004**
Interpersonal	31.50	23.67	13.11	18.79	2	.000**
Play	28.07	23.61	15.66	8.61	2	.013*
Coping Skills	28.50	22.11	16.05	8.34	2	.015

*** A Bonferroni correction of 0.006 was used to avoid type I errors; *significant at 0.01*

Relationships between the Vineland Adaptive Behaviour Scale (VABS) and the Slossen Intelligence Test – Revised (SIT-R3)

A Pearson correlation was conducted to explore the inter-relationship between the Vineland Adaptive Behaviour Scale (VABS) and Slossen Intelligence Test- Revised (SIT-R3). Strong correlations were reported on the Communication, Socialisation and Daily Living Skills domains, indicating that cognitive intelligence was significantly related. Interestingly, the overall relationship between the Adaptive Behaviour Composite and SIT-R was weak and table 5.6.3 summarises these findings.

Table 5.6.3 Pearson correlation exploring the relationship between the Vineland Adaptive Behaviour Scale (VABS) and Slossen Intelligence Test (SIT-R3).

VABS Domain & Sub-Domain	SIT-R. MAE in Months
Adaptive Behaviour Composite	.13
Expressive Language	.66
Receptive Language	.52
Written	.58
Communication Domain	.73
Personal	.67
Domestic	.51
Community	.63
Daily Living Skills Domain	.71
Interpersonal Skills	.63
Play	.59
Coping Skills	.39
Socialisation	.73

The impact of visual acuity on the Domain and Sub Domains of the Vineland Adaptive Behaviour Scale for children with isolated Hypopituitarism, SOD and ONH

Table 5.6.4 summarises that significant differences were reported on the level of visual acuity and the domains of Daily Living Skills and Socialisation.

Table 5.6.4 Differences between the level of vision and the ABC Mean Age Equivalent scores and domain scores on the VABS.

VABS Domain & Sub-domain level	Visual Acuity	Mean (SD)	*F*	*df*	*p-value*
Adaptive Behaviour Composite (ABC)	Normal	84.87 (33.41)	336	3,39	.799
	Impaired	75.36 (51.56)			
	Severe	79.30 (24.71)			
	Profound/blind	92.38 (31.05)			
Communication	Normal	129.53 (55.48)	2.050	3,39	.123
	Impaired	96.45 (46.08)			
	Severe	99.38 (53.54)			
	Profound/blind	82.50 (19.16)			
Daily Living Skills **	Normal	106.00 (43.63)	4.71	3,39	.007
	Impaired	85.00 (41.38)			
	Severe	44.88 (33.15)			
	Profound/blind	85.33 (41.93)			
Socialisation Skills* *	Normal	130.73 (42.01)	5.98	3,39	.002
	Impaired	97.82 (43.54)			
	Severe	90.38 (28.68)			
	Profound/blind	66.38 (11.78)			

*** A Bonferroni correction of 0.017 was used to avoid type I errors; *significant at 0.05*

Post-hoc analysis using Bonferroni corrections showed a statistically significant difference between the mean age equivalence of the Daily Living Skills and the

Socialisation domain for children with normal vision when they were compared to children with profound visual loss and complete blindness.

The impact of visual acuity on the Slossen Intelligence Test Revised (SIT-R3) for children with isolated Hypopituitarism, Septo-Optic Dysplasia and Optic Nerve Hypoplasia

There were also significant differences between the level of vision and the Slossen Intelligence Tests Revised mean age equivalent scores (SIT-R3) (F (3, 39) =5.41, p = 0.003 partial eta squared 0.31). Post-hoc analysis using Bonferroni corrections indicated the mean SIT- R3 scores for children with normal vision was significantly different (M = 137.33, SD = 48.94), to children with impaired vision (M= 88.00, SD = 32.17), and children with a profound visual impairment (M = 73.13, SD = 24.03). Children with a severe visual impairment did not significantly differ from children with normal, impaired or a profound visual impairments (M= 106.37, SD = 44.11). However, using the mean age Adaptive Behaviours Composite as a covariate no significant differences were reported (F (3, 39) =.043, p =.84 partial eta squared 0.01). Thus, indicating that intellectual disability rather than visual impairments influenced cognitive ability in children.

The impact of Autistic Spectrum Disorders on the Domain and Sub Domains of the Vineland Adaptive Behaviour Scale

There were no reported statistically significant differences between children on the Socialisation, Communication domain, or the Adaptive Behaviour Composite mean age equivalences of the Vineland Adaptive Behaviour Scale. Statistically significant

differences were reported on the Daily Living Skills, Expressive Language Domain and the Interpersonal and Community sub-domain of the Vineland Adaptive Behaviour Scale and table 5.6.5 summarises these findings.

Table 5.6.5: Differences between children who scored above/below the cut off-point on the SCQ and the Vineland Adaptive Behaviour Scales

VABS Domain Sub-Domain	SCQ	Mean	SD	*F*	df	*p-value*
Receptive Language	-	34.97	6.38			
	+	20.16	5.59	1.12	42	.295
Expressive Language	-	59.51	10.87			
	+	29.75	8.25	17.63	42	.000**
Written	-	50.41	9.20			
	+	55.98	15.53	.092	42	.763
	-	49.89	9.11			
Communication	+	41.01	11.37	1.90	42	.175
Personal	-	51.89	9.47			
	+	15.72	4.36	11.68	42	.001**
Domestic	-	57.33	10.47			
	+	35.27	9.78	2.644	42	.112
Community	-	49.01	8.95			
	+	22.35	6.20	4.531	42	.039*
	-	41.21	7.52			
Daily Living	+	22.77	6.32	4.82	42	.034*
Interpersonal	-	51.62	9.42			
	+	36.96	10.25	6.51	42	.015**
Play	-	50.49	9.22	.		
	+	42.09	11.67	745	42	.393
Coping	-	51.43	9.39			
	+	35.40	9.82	3.16	42	.083
	-	40.21	7.34			
Socialisation Domain	+	20.22	5.61	1.90	42	.175
Adaptive Behaviour Composite	-	41.89	7.65			
	+	41.66	11.56	.013	42	.909

***p < 0.01; * p <0.05; N =12 (+) ASD = scoring <15 of SCQ (-), N = 30 Non ASD = scoring >15 SCQ*

Differences between age equivalent scores of the Slossen Intelligence Test children scoring above/below the cut off for Autism Spectrum Disorders on the Social Communication Questionnaire

Table 5.6.6 shows that there were also significant differences between children who scored above the cut off point for Autistic Spectrum Disorders and those who did not score above the cut-off point on the SCQ for the Slossen Intelligence tests mean age equivalent scores. The mean scores of children with suspected autism were considerably lower than children without autistic behaviours

Table 5.6.6: Differences between age equivalent scores of the Slossen Intelligence tests children scoring above/below the cut off for Autism Spectrum Disorders on the SCQ

SCQ	Slossen Intelligence Test-Revised				
	Mean	SD	*t*	*df*	*p-value*
-	117.67	45.56	3.19	1	.003
+	76.69	35.00			

N =12 (+) ASD = scoring <15 of SCQ (-), N = 30 Non ASD = scoring >15 SCQ

5.6 Discussion

The present study is the first to provide descriptions of the adaptive and cognitive profiles of children with Septo Optic Dysplasia, Optic Nerve Hypoplasia, and isolated Hypopituitarism. Chapter Five aimed to profile the Cognitive and Adaptive behaviours of children with Septo Optic Dysplasia and Optic Nerve Hypoplasia. Furthermore, it also investigated the relationship between the adaptive and cognitive

profiles of children with Septo Optic Dysplasia and Optic Nerve Hypoplasia and their autistic phenomenology.

Differences between children with isolated Hypopituitarism, Septo Optic Dysplasia and Optic Nerve Hypoplasia on the Adaptive Functioning and domain levels of the Vineland Adaptive Behaviour Scale

Overall, the Adaptive Behaviour Composite level of the Vineland Adaptive Behaviour Scale reported no differences between children with Septo Optic Dysplasia, Optic Nerve Hypoplasia and isolated Hypopituitarism after the removal of children with profound intellectual disability. However, at domain level, statistically significant differences were reported. At the conservative alpha value of 0.017, only the Socialisation Domain reported statistically significant differences between the three clinical cohorts. Children with Septo Optic Dysplasia showed the greater impairments in the sub-domain of Receptive Language of the Vineland Adaptive Behaviour Scale, which assesses how children learn to listen, and understand language. These children also showed the greatest impairment in the sub domain of Interpersonal Skills of the Vineland Adaptive Behaviour Scale, which assesses imitation, and the showing of emotions, in comparison to children with Optic Nerve Hypoplasia and isolated Hypopituitarism. The findings of this investigation endorse the use of fine grained approach to the analyses of adaptive behaviours.

The level of visual acuity was found to differ significantly on all domains and sub-domains of the Vineland Adaptive Behaviour Scales, children who were completely blind scored lower than children with a visual impairment. However, post-hoc tests

revealed no differences between children with impaired vision and blindness. Differences between cognitive intelligence and visual acuity showed that blind children had the lowest intelligence scores, but when the Adaptive Behaviour Composite was included as a covariate this effect was absent, indicating children with Septo Optic Dysplasia and Optic Nerve Hypoplasia are similar, as they share the similar group characteristics of visual loss and developmental delays.

The differences between the Adaptive and Cognitive profiles of children with or without autism

There was strong relationship between the domains of the Vineland Adaptive Behaviour Scale and the Slossen Intelligence Scale Revised, but not on the Adaptive Behaviour Composite of the Vineland Adaptive Behaviour Scale. This suggests that both cognitive and adaptive behaviours are interrelated and need to be assessed when looking at autistic phenomenology.

The study also suggests, that particular aspects of adaptive behaviour, such as Expressive Language Skills, Personal Skills, Community, Daily Living Skills and Interpersonal Skills are statistically different between non autistic, and autistic children. Differences were also reported on the Slossen Intelligence Test between autistic and non autistic children.

Overall, significant variability in the functioning of children across cognitive and different behavioural domains was found. The results demonstrate the importance of not relying on a single measure of intellectual disability, as derived from the Adaptive Behaviour Composite of the Vineland Adaptive Behaviour Scale, but also

using the domains and sub-domains of the Vineland Adaptive Behaviour Scale, when assessing children's developmental profiles, and this would help to identify specific impairments in children.

The findings of the present study are in line with early research, which has reported that autistic disorders are over represented in children with lower levels of cognition (Wing & Gould, 1979). In support, to the Carter *et al.*, (1998) study, children with Optic Nerve Hypoplasia and Septo Optic Dysplasia who displayed autistic tendencies did show lower scores on the Socialization domain, but in contrast, they showed intermediate scores on the Daily Living Skills domain and the highest scores on the Communication domains when age equivalent scores were applied. Previous research (Volkmar *et al.*, 1987) and the current findings support that children's cognitive and adaptive abilities can be significant predictors for the severity of their autistic symptomology.

Implications, future suggestions, and Summary of the present study

Whether early educational interventions may have impacted children's cognitive and adaptive functioning was not known for the present study, and could have impacted the results of the study. More importantly, if improvements could have been detected in the adaptive and cognitive profiles of children, this would further endorse the importance of early diagnosis of autism, and the influence of early interventions. The study highlights the need for appropriate educational provisions for children with Septo Optic Dysplasia and Optic Nerve Hypoplasia.

CHAPTER SIX

THE ASSESSMENT OF SENSORY IMPAIRMENTS, AND MALADAPTIVE BEHAVIOURS IN CHILDREN WITH SEPTO OPTIC DYSPLASIA, OPTIC NERVE HYPOPLASIA AND ISOLATED HYPOPITUITARISM

6.1 Background to Chapter Six

The literature review and the empirical components of the thesis, have both reported that children with Septo-Optic Dysplasia and Optic-Nerve Hypoplasia are vulnerable to autistic phenomenology, and this vulnerability is closely related to children's degree of intellectual disability and/or visual loss. Children who reported with autistic phenomenology in Chapter Four, showed the classic autistic type impairments in their Social Interaction and Communication. Using the Social Communication Questionnaire, Chapter Four reported at item level the presence of sensory processing impairments, Restrictive, Repetitive and Stereotyped behaviours, and Self Injurious behaviours in a number of children Septo-Optic Dysplasia and Optic-Nerve Hypoplasia.

The presence of "Restricted, Repetitive and Stereotyped patterns of behaviour, interests, and activities" is one of the three essential criteria needed for the diagnosis of autism by a Clinician (DSM-IV-R; APA, 2000). The present thesis did not examine the presence of these behaviours in detail during Chapter Four, as children with intellectual disability and/or visual loss commonly display this symptomatology, which is not always indicative of autistic phenomenology (Cunningham & Schreibman, 2007; Rojahn & Sisson, 1990). This ensured that autistic disorders were not over represented in the present thesis, due to overlapping symptomatology between autism, visual loss and intellectual disability.

Restrictive, Repetitive and Stereotyped behaviours can pose serious problems for parents, educational and medical professionals, as they are most often inappropriate in most situations, and they can interfere in children's everyday activities. Commonly, Self-Injurious behaviours can also present alongside Restrictive, Repetitive and Stereotyped behaviours in children, and research has shown that both of these set of behaviours are highly correlated with one another (Bodfish *et al.*, 1995). For such reasons, some researchers consider Self-Injurious behaviours as a "substrate of stereotyped behaviours" (Gorman-Smith & Matson, 1985). For such reasons, Self-Injurious behaviours and Restrictive, Repetitive and Stereotyped behaviours are commonly referred to collectively as maladaptive behaviours.

Maladaptive behaviours have been reported in children with Fragile X syndrome (Goldstein & Reynolds, 1999), Williams's syndrome (Gillberg & Rasmussen, 1994), Prader-Willi syndrome (Dimitropoulos & Schultz, 2007), Down syndrome (Hepburn & MacLean, 2009), Angelman Syndrome (Peters, Beaudet, Madduri, & Bacino, 2004), Obsessive Compulsive Disorder (Leornard *et al.*, 1990), Tourettes Syndrome (Cath *et al.*, 2001) and children with an intellectual disability with no specified aetiology (Tonge & Einfeld, 2003).

A further impairment which is strongly associated with Autistic Spectrum Disorders is children's unusual responses to sensory inputs, and this phenomenon has also been found to correlate strongly with Restrictive, Repetitive and Stereotyped behaviours, but not with children's Social or Communicative impairments (Rogers, Hepburn, & Wehner, 2003). Some researchers consider Restrictive, Repetitive and Stereotyped behaviours an antecedent of a sensory processing disorders (Ornitz, 1989), whereas others argue that Restrictive, Repetitive and Stereotyped behaviours and sensory processing disorders are co-morbid with one another (Rogers, Hepburn, & Wehner,

2003). Based on previous literature and the findings of Chapter Four the measurement of Restrictive, Repetitive and Stereotyped behaviours, Self Injurious Behaviours and Sensory Processing disorders warranted further investigation.

6.2 Overview of Chapter Six

Autistic-like features or "blindisms" observed in children with severe to profound visual loss (e.g. eye-pressing, light gazing, flicking fingers in front of the eyes, rocking, spinning and twirling (Warren 1986) are considered to be due to a loss of sensory input and secondary difficulties in expressive ability (Fraiberg, 1977). In addition, communication abnormalities, self-isolation, abnormal play which were described in Chapter Three, may be substituted by maladaptive behaviours in order to offer children with a source of sensory stimulation (Carvill & Marston, 2002).

Drawing upon this viewpoint the present Chapter will describe the occurrence of sensory processing disorders and maladaptive behaviours in children with "isolated" Hypopituitarism, Septo Optic Dysplasia and Optic Nerve Hypoplasia. Chapter Six will begin to consider whether children's varying degrees of visual impairments and/or associated intellectual disability increases children's vulnerability to these behavioural characteristics of Autistic Spectrum Disorders. The empirical component of the thesis will firstly assess sensory processing disorders in children with Septo-Optic Dysplasia and Optic-Nerve Hypoplasia in comparison to children with isolated Hypopituitarism. To address the primary objective of the thesis, Chapter Six will examine the reported presence of Restrictive, Repetitive and Stereotyped behaviours in the child clinical cohort. Lastly, this Chapter will identify the occurrence and types of reported Self Injurious Behaviours in children with Septo-Optic Dysplasia and Optic-Nerve Hypoplasia.

6.3 Literature review on Restrictive, Repetitive and Stereotyped Behaviours

Research into children's Restrictive, Repetitive and Stereotyped Behaviours has not received as much attention, in comparison to research into children's social and communication impairments, even though such behaviours are commonly reported by caregivers (South, Ozonoff, & McMahon, 2005; Russell, 1997).

Stereotypy, such as repetitive body rocking, hand flapping, or use of the body to generate object movements (e.g., plate spinning, string twirling) are prevalent in children with autistic disorders. In a study of 224 autistic children, Campbell *et al.*, (1990) reported that all children showed some stereotypy's, with 25% displaying object stereotypy, 16% hand flapping, 15% body rocking, 12% head tilting, 28% other lower extremity, and 18% other upper extremity.

Autistic children can also show intense preoccupations with elements of their environment such as colour, lights, transport and containers. Similarly, a child might be obsessed with learning all about computers, television programs, lighthouses or other topics. Szatmari *et al.*, (1989) reported that 86% of autistic children with normal IQ, 37% of children with Asperger's syndrome, and only 9% of the control group demonstrated such circumscribed interests.

Restricted and stereotyped patterns of interest, or the need for sameness can involve a persistent fixation on parts of objects or an inflexible adherence to specific, non functional routines or rituals. The high co-morbidity rate of Autistic Spectrum Disorders and intellectual disability sometimes masks the particular phenotype of Restricted, Repetitive Behaviours in children with Autistic Spectrum Disorders. In some cases, Restricted, Repetitive Behaviours are better accounted for as a consequence of an intellectual disability, or a sensory impairment, rather than Autistic Spectrum Disorders, or vice versa. Even so, intellectual disability is often correlated with particular types of

Repetitive Behaviours in autistic individuals. Often, autistic individuals with low cognitive abilities are more likely to exhibit insistence of sameness, whereas autistic individuals with average intelligence tend to display significantly more ritualistic behaviours, although, both groups usually present with high levels of circumscribed interests (Bartak & Rutter, 1976). Sensory and repetitive motor behaviours are more commonly displayed in autistic children with lower cognitive abilities, while complex repetitive activities or repetitive speech are more commonly reported in autistic children with higher cognitive abilities (Militerni, Bravaccio, Falco, Fico & Palermo, 2002). Baron-Cohen and Wheelwright (1999) shed light on this difference, were they reported that children with Autistic Spectrum Disorders exhibited "obsessions" more in the domain of "folk physics" (an interest in how things work), and significantly less in the domain of "folk psychology" (an interest in how people work), when compared to children with Tourette syndrome.

Using the Autism Diagnostic Interview-Revised (ADI-R: Lord, Rutter, & Le Couteur, 1994), Richler, Bishop, Kleinke, & Lord (2007), compared the Restrictive Repetitive behaviours of 165 children with Autistic Spectrum Disorders, to forty-nine children with developmental disorders, and sixty-five children typically developing children at the age of two years. A factorial analysis reported more Restrictive Repetitive behaviours in children with Autistic Spectrum Disorders. In addition, autistic children's Restrictive Repetitive behaviours were more frequent and severe, than the other two groups of children. Robin *et al.*, (2005) explored the relationships between Restrictive Repetitive behaviours and associated clinical features (i.e. cognitive and adaptive functioning levels, sleep problems, medication use, and other behavioural problems) in two groups of children with Autistic Spectrum Disorders (high nonverbal IQ $\geq$ 97 versus and low nonverbal IQ $\leq$50). For the group as a whole, nonverbal cognitive ability,

adaptive functioning level, the presence of sleep problems, and three scales of; Irritability, Lethargy, and Hyperactivity from the Aberrant Behaviour Checklist (ABC; Aman & Singh, 1986) were highly correlated with total scores on the Repetitive Behaviour Scale-Revised (RBS-R; Bodfish *et al.*, 1999). Furthermore, a significantly higher prevalence of Sameness of Behaviours in the low non-verbal IQ group was demonstrated in comparison to the high functioning group of children. Similarly, Bartak and Rutter (1976) found higher incidences of Sameness of Behaviours in lower functioning autistic children, when compared to higher functioning autistic children. In further support, Bak, (1999) reported strong correlations between the severity of Stereotypies and intellectual disability, Receptive and Expressive Language Skills.

Turner (1999) has distinguished between ''lower-level'' (e.g., stereotyped motor movements) and ''higher-level'' (e.g., rituals, circumscribed interests) repetitive behaviours. Lower-level classes of repetitive behaviour are not specific to autism, but low IQ and higher-level behaviours, such as circumscribed interests are restricted to autism spectrum disorders. In contrast, Bodfish *et al.*, (2000) proposed an ''overall response class'' (Bodfish *et al.*, 2000, p. 242), as the co-morbidity of repetitive behaviour across a variety of disorders, and syndromes suggest a common pathophysiology for all classes of repetitive behaviour.

Repetitive behaviours in children with visual loss

Several researchers have noted high incidences of repetitive behaviours in children with severe and profound visual loss, however many of these children also present various degrees of intellectual disability (Bak, 1999; Fazzi *et al.*, 1999; Hallenbeck 1954a; Keller 1958; McHugh & Lieberman, 2003; Shaffer, Dale & Salt, 2008; Tröster *et al.*, 1991; Tröster, Brambring, & Beelmann, 1991).

The prevalence of Restrictive, Repetitive and Stereotyped behaviours in the children with Optic Nerve Hypoplasia and Septo Optic Dysplasia was recently reported as between 25%-45% in the retrospective study carried out by Shaffer *et al.,* (2008). More specifically, eye poking and pressuring the eyeball, appear to be relatively specific to children with visual impairments, especially those with an intact optic nerve but a damaged cornea (Troster *et al.*, 1991). Body Rocking, for example, appears to be strongly associated with retinopathy of prematurity (Jan, Freeman, & Scott, 1977; McHugh & Lieberman, 2003).

It has been argued that stereotypes may have a functional value for children who are blind, compared to sighted autistic children (Troester, Brambring, & Beelmann, 1994). For sighted autistic children, repetitive behaviours provide sensory stimulation, by increasing arousal levels when stimulation from the environment is low (Baumeister, 1978; Forehand & Baumeister, 1971). However, children with visual loss may use repetitive behaviours to make sense of their world by aiding exploration of their immediate environment (Gense & Gense, 2004).

General theories of Repetitive Behaviours

Repetitive behaviours have shown to be heterogeneous in their typography but also indiscriminate, as they occur in children with autistic disorders, sensory impairments and intellectual disability (Cunningham & Schreibman, 2007). More so, regardless of the disorder that children present with, similar phenomenology are expressed, although the motivations and pathway to Restrictive Repetitive behaviours may be very distinct and unique according to children's syndrome characteristics. By addressing the theories put forward to explain repetitive behaviours, it is anticipated that this may aid in the understanding of children's motivations towards repetitive behaviours.

O'Gorman (1967) and Rimland (1964) have proposed that repetitive behaviours in children with autism function as a coping mechanism in unpredictable environments, and individuals with autism focus their efforts on these behaviours in order to control some aspect of their environment. Evans and Gray (2000) have report that the basal ganglia, and more specifically, the caudate nucleus, may be involved in repetitive behaviours. The over-activity of the basal ganglia is thought to be responsible for abnormal obsessions and compulsions (Baxter, 1992).

Lovas *et al.*, (1979) proposes that "stimulus over selectivity" accounts for many of the preoccupations or fixations autistic children possess. It suggests that individuals will fixate on small features, but not on the holistic nature of the object or activity, to avoid over arousal. In support of this theory, repetitive behaviours persist through development because they provide sensory stimulation, according to the Baumeister's (1978) Homeostatic theory, as they increase arousal levels when stimulation from the environment is low (Baumeister, 1978; Forehand & Baumeister, 1971). It has been proposed that stereotyped movements are, in fact, adaptive because they help under- or over stimulated children to maintain an optimal or homeostatic state of stimulation (Miller, Lane, Cermak, Anzalone, & Osten, 2005).

Alternatively, neural pathways for either oxytocin or vasopressin could also account for many aspects of autism including the repetitive behaviours, (Insel, O'Brien & Leckmanl, 1999; Insel & Young, 2001). Repetitive behaviours in autism, and the severity of these core symptoms have also been linked to abnormal serotonin function (5HT1d sensitivity) (Hollander *et al.*, 2000) and specifically, B cell immune marker (D8/17) (Hollander *et al.*, 1999).

To summarise these theories, Berkson (1996) using factor analytic studies of several measures of behaviours and concluded that research to date is inconsistent with

the notion of a general factor, and it is argued that several orthogonal factors exist. However, total or near-total visual loss leads to a more generalized dysfunction in sensory processing as a partial consequence of the absence of visual stimulation (Gal, 2006), therefore, when considering the presence of Restrictive, Repetitive and Stereotyped behaviours in children with visual loss the occurrence of sensory processing disorders must be assessed.

6.3.1 Literature review sensory processing disorders

The criteria for autism in the DSM-III (APA, 1980) included lack of social responsiveness, impairments in communication, and bizarre responses to the environment, which included atypical sensory responses. With the publication of the DSM-III-R (APA, 1987), the criteria for autism was altered and it became focused upon individual's restricted repertoire of activities and interests, rather than unusual sensory responses. The characteristic of unusual sensory responses was removed from the diagnostic criteria and was considered as only an associated feature of autistic disorders.

Sensory processing disorders have been categorised by Miller *et al.*, (2005) into three sub types. Firstly, "sensory modulation disorder", describes difficulties in regulating and organizing the type and intensity of responses to sensory input (Miller, Anzalone, Lane, Cermak, & Osten, 2007). Secondly, "sensory discrimination disorder", describes an individual's impairments in processing the spatial and temporal qualities of touch, movement, or body position; vision and audition, (Koomar & Bundy, 2002). Lastly, "sensory based motor disorder", describes an individual's difficulties with posture and motor planning. This usually exhibits as clumsiness, poor gross motor, fine motor and manipulation skills Children can show difficulties with balance, sequencing movements, bilateral coordination, and imitating movements (Miller *et al.*, 2005).

The use of parental reports in research has helped to identify the presence of specific patterns of sensory impairments in children with autism (Baker, Lane, Angley & Young, 2007; Lord, Rutter & Le Couteur, 1994; Wing & Gould, 1979). Using the Diagnostic Interview for Social and Communication Disorders (DISCO; Wing, Leekham & Gould, 2002), Leekham *et al.*, (2006) reported that over 90% of children with autism showed sensory abnormalities. Baker, *et al.*, (2007) further reported significant relationships between sensory processing and social, emotional and behavioural functions. Baranek (2006) also reported in a group of autistic individuals, that 69% of the group demonstrated sensory impairments specifically, hypo responsiveness to both social and non-social situations, suggesting that sensory impairments were independent of social interaction or communication.

Furthermore, severity and frequency of sensory impairments have been identified as being related to chronological age and developmental delays (Baranek 2006; Leekham *et al.*, 2006). A meta-analysis performed by Rogers and Ozonoff (2005), on forty-eight empirical papers and twenty-seven theoretical or conceptual papers reported that sensory symptoms were only more frequent and more prominent in children with autism when compared to typically developing children. However, there was no evidence to show sensory impairments differentiated autism from other developmental disorders.

Studies included in the meta-analysis, such as Rogers, Hepburn and Wehner (2003) reported from a group of children with either autism, Fragile X syndrome, developmental disabilities of mixed aetiology, or typically development, that children with Fragile X syndrome and autism were significantly more impaired on the Short Sensory Profile (Dunn, 1999) than were typically developing children and children with developmental disabilities. Children with autism did not differ significantly from children with Fragile X syndrome. Correlation analyses also indicated that neither overall

developmental level nor IQ was related to abnormal sensory scores but significant relationships with overall adaptive behaviours were reported.

Similarly, Miller *et al.*, (1999) reported that the sensory profiles of children with autism, Fragile X Syndrome and Sensory Modulation Disorder did not differ. However, Ben-Sasson., Hen, Fluss, Cermak, Engel-Yeger and Gal (2009) analysed the results of fourteen studies which mostly reported significant differences between autistic children and typically developing children. Autistic children generally showed hypo sensitivities, followed by hyper responsivity and sensation seeking. Variability was reduced when chronological age, severity of autism, and type of control group was statistically controlled.

Drawing parallels from studies examining quasi-autistic features in Romanian children who had suffered extreme deprivation and comparing them with blind children, similar sensory impairments have been reported, with most maladaptive behaviours declining after adoption, but with the exception of unusual sensory responses, which demonstrates the permanence of sensory processing disorders (Rutter *et al.*, 1999; 2001).

When children present with a combination of autism, visual loss and/or intellectual disability, it becomes increasingly difficult to establish the origin of the observed sensory processing disorders or maladaptive behaviours. Rimland (1964) and Delacato (1974) both suggest that sensory impairments are an antecedent of autistic phenomenology, rather than an associated feature of autism and, drawing from this viewpoint, Gibbons (2005), suggests that if the origin of autistic behaviours is viewed as a result of abnormal perception, this may explain some of the frequently observed autistic-like behaviours in the blind. Similarly, Andrew and Wyver's (2005) question whether blind children, follow a different pathway to autistic behaviours to that of sighted autistic children.

Children with visual impairments, genetic syndromes and/or intellectual disability can show similar sensory processing disorders to that of autistic individuals (Kern *et al.*, 2007; Talay-Ongan & Wood, 2000). However, the reasons for these sensory impairments can be different, depending on the origin and the types of neurodevelopmental disorders that children have.

6.3.2 Literature review on Self-Injurious Behaviours

Self-injurious stereotyped movements are rarely evident among typical children, but have been reported in 52% of children with visual impairments (Gal, Dyck, & Passmore, 2009). It has been proposed that stereotyped movements are adaptive because they help under- or over stimulated children to maintain an optimal or homeostatic state of stimulation (Miller, Lane, Cermak, Anzalone, & Osten, 2005). Reports of the incidence of Self Injurious Behaviours in children with developmental disability range from 3% to 46%, with head banging, head and body hitting, eye gouging, biting, and scratching being the most common of these behaviours (Bodfish, Crawford, Powell, *et al.*, 1995). The occurrence of Self Injurious Behaviours can differ according to children's degree of intellectual disability, with 2.6% of children with a mild disability, 3.4% of children with a moderate disability, 7.1% of children with a severe disability, and 16.9% of children with a profound intellectually disability displaying forms of Self Injurious Behaviours (Jacobson, 1982).

The assessment of Self Injurious Behaviours in children with visual impairments has received little attention from researchers and professionals (Van Hasselt, Kazdin & Hersen, 1986), compared to the measurement of Self Injurious Behaviours in children with Autistic Spectrum Disorders, and/or intellectual disability (Bartak & Rutter, 1978; Kiernan & Kiernan, 1987; Oliver; 1995). Even in spite of the differential diagnosis

children may receive for their neurodevelopmental disorders, all Self Injurious Behaviours share a common component for children, as Self Injurious Behaviours often appear to be meaningful acts, which relate to the needs, and wants of a child. However, this often leads to a child finding an effective, but maladaptive strategy to aid communication of their emotional or physical state, and ultimately control of their immediate environment (Maclean-Wood, 2003).

A number of theories have been proposed which try to explain some of the motivations for Self Injurious Behaviours in children with autism and/or intellectual disability, but they differ when interpreting whether self injury is a replacement form of communication or due to neurochemical or biological alterations of the brain.

Self-Injurious Behaviour has also been associated with seizure activity in the frontal and temporal lobes (Gedye, 1989; Gedye, 1992). The under-arousal theory states that some individuals function at a low level of arousal and engage in self-injury to increase their arousal level (Edelson, 1984; Baumeister & Rollings, 1976). In contrast, the over-arousal theory states that some individuals function at a very high level of arousal (e.g., tension, anxiety) and engage in self-injury to reduce their arousal level. Another reason why an individual may engage in head banging is to reduce pain, such as pain from a middle ear infection or a migraine headache (de Lissovoy, 1963; Gualtieri, 1989). There is growing evidence that pain associated with gastrointestinal problems, such as acid reflux and gas, may also be associated with self-injury (Moss, Oliver, Hall, Arron, & Sloneem, 2005).

Excessive self-rubbing or scratching may be an extreme form of self-stimulation as a child may not feel normal levels of physical stimulation; and as a result, he/she damages the skin in order to receive stimulation or increase arousal (Edelson, 1984). Caregivers and parents often report that the child's self-injury is a result of frustration.

This is consistent with the traditional "Frustration – Aggression" model proposed by Dollard and his colleagues (1939). Commonly reported scenarios include, a person with poor communication skills becoming frustrated because of his/her lack of understanding of what was said to him/her (poor receptive communication) or because the caretaker does not understand what is said/requested; or an individual who has good communication skills but does not get what he/she wants (Symons, 1995).

Communication problems have often been associated with self-injurious behaviour. For instance, if a person has poor receptive and/or has poor expressive language skills, then this may lead to frustration and escalate into self-injury. Furthermore, Lovaas (1987) found that the frequency of self-injury could be controlled by manipulating social consequences (Lovaas & Simmons, 1969). Lovaas (1987) found that positive attention increased the frequency of self-injury (i.e., positive reinforcement), whereas ignoring the behaviour decreased the frequency of Self Injurious behaviors (i.e., extinction).

Another reason why an individual may engage in Self-Injurious Behaviour is to obtain an object or event (Durand 1986; Durand & Crimmins, 1988). For instance, an individual may request something, not receive it, and then engage in Self-Injurious Behaviour. Additionally, the behavior may be reinforced positively if the individual should, on occasion, receive the desired object or event. A survey by Maisto, Baumeister, and Maisto (1978) reported that 33% of the clients engaged in self-injury because "they wanted something".

Some individuals engage in self-injury to avoid or escape an 'aversive' social encounter (Carr Newson & Binkoff, 1976; Edelson Tubman & Lovaas, 1983). The individual may engage in self-injury just prior to the social interaction; and thus, he/she

may avoid the social interaction before it begins. Alternatively, the individual may engage in self-injury to escape (or terminate) a social encounter that has already begun.

Summary of the aims of Chapter Six

In summary, when children exhibit severe to profound levels of visual impairment, their hypo or hypersensitivities to the processing of sensory stimuli through their intact senses may manifest as the observed maladaptive behaviours reported in Chapter Four and previous research. Maladaptive behaviours, ultimately serve to increase stimulation in an under stimulating environment or to block excessive stimulation from a child's intact senses (Mason, 1991).

As children with Septo-Optic Dysplasia and Optic Nerve Hypoplasia, can exhibit both visual impairments and intellectual disability it is not known which of these two syndrome characteristics has more of an impact on Restrictive Repetitive and Stereotyped behaviours, Sensory Processing Disorders, or Self Injurious Behaviours, and Chapter Six will address this.

For these reasons the present study aims to explore:

- The reported differences between children with Septo-Optic-Dysplasia, Optic Nerve Hypoplasia and isolated Hypopituitarism Repetitive and Stereotyped behaviours using the Social Communication Questionnaire, Gilliam Autism Rating Scale and the Autism Diagnostic Observation Schedule.
- Using the Short Sensory Profile (Dun, 1999), the differences between children with Septo-Optic-Dysplasia, Optic Nerve Hypoplasia and isolated Hypopituitarism Sensory Processing Profiles. Specifically, the analysis will

aims to examine, whether Autistic Spectrum Disorders, intellectual disability and/or visual loss, better account for the sensory impairments which have been anecdotally reported by parents in these syndrome groups.

- Knowing that, both autistic phenomenology and varying degrees of intellectual disability and/or visual loss are prevalent in children with Septo-Optic Dysplasia and Optic Nerve Hypoplasia, it would be expected that these children have an increased vulnerability to Self Injurious Behaviours. Therefore, the present investigation will be the first to assess the occurrence and types of Self-Injurious Behaviours displayed by children with these two conditions.

6.4 Methods

Measures

Measures used for the assessment of Restrictive, Repetitive and Stereotyped Behaviours

The Autism Diagnostic Observation Schedule (ADOS; Lord *et al.*, 2002) is a semi-structured standardised assessment of communication, social interaction and play or imaginative use of materials. Previous research has shown that impairments in these behavioural domains are crucial indicators of suspected autistic tendencies in children (Lord *et al*, 1998). The schedule also examines speech abnormalities, stereotyped and restricted interests. However, the Autism Diagnostic Observation Schedule does not utilize impairments in these areas for diagnosis of autism, mainly because these behaviours frequently occur in children with learning disabilities and/or visual impairments.

Gilliam Autism Rating Sale (GARS; Gilliam, 1995)

The Gilliam Autism Rating Scale (GARS; Gilliam, 1995) helps to identify and diagnose autism in individuals from the age of three through to twenty-two years of age.

Items on the Gilliam Autism Rating Scale are based on the definitions of autism adopted by the Autism Society of America and the Diagnostic and Statistical Manual of Mental Disorders. The items are grouped into four subtests: stereotyped behaviours, communication, social interaction, and developmental disturbances.

Social Communication Questionnaire (SCQ; Rutter, Bailey, Berument, LeCouteur, Lord & Pickles, 2003)

The Social Communication Questionnaire is a screening questionnaire for Pervasive Developmental Disorders (PDD). This brief instrument helps evaluate communication skills, social functioning and repetitive behaviours in children who may have Autistic Spectrum Disorders.

The Vineland Adaptive Behaviours Scales (VABS; Sparrow, Balla, & Cicchetti, 1984)

The Vineland Adaptive Behaviours Scales (VABS; Sparrow *et al.*,1984) measures four domains of adaptive behaviours: communication, with sub-domains in Receptive, Expressive and Written skills; Daily Living Skills, with further sub domains in Personal, Domestic and Community skills; Socialisation, including Interpersonal Relationships, Play and Leisure and Coping Skills; and for those below six years, Fine and Gross motor skills.

Measures used for the assessment of Sensory Processing Disorders

The Short Sensory Profile (SSP; Dunn, 1999)

The Short Sensory Profile (SSP; Dunn, 1999) was designed as a screening tool to determine how well children process sensory information in everyday situations. It consists of thirty-eight questions about children's Tactile Sensitivity, Taste/Smell

Sensitivity, and Movement Sensitivity, Under-responsiveness/Sensation Seeking, Auditory Filtering, Low Energy/Weak and Visual/Auditory Sensitivity.

The Short Sensory Profile also allows for the classification of Sensory Scores into three categories of; "Typical Performance", "Probable Difference" and "Definite Differences" in sensory processing. Children, who score between 190-155, are described as "typical"; scores between 154-142 indicate a "probable difference" and scores below 141 indicate a "definite difference" in children's processing of sensory information. For the present study, three questions which assessed Visual Sensitivity were removed for all children. The removal of these questions was required due to the levels of visual loss, which is often observed in children with Septo Optic Dysplasia and Optic Nerve Hypoplasia. The adapted classification of Short Sensory Profiles scores for all children in Study Six was; 175-140, for children who showed "Typical" sensory profiles, scores between 139-127 indicated a "Probable Difference" and scores below 126 indicated a "Definite Difference" in children's processing of sensory information.

Caregivers are asked to check the box that best describes the frequency with which the subject engages in the listed behaviours. Choices are: never (five points); seldom (four points); occasionally (three points); frequently (two points); and always (one point). It is important to note that, on the Sensory Profile, lower scores indicate greater symptoms. The Sensory Profile includes high and low threshold items. High threshold items measure an individual's lack of response or need for more intense stimuli. Low threshold items measure a person's notice of or annoyance with sensory stimuli. The Sensory Profile has reported good psychometric properties with the Cronbach's Alpha for internal consistency ranging from 0.47 to 0.91 and internal validity correlations ranged from 0.25 to 0.76 (Dunn, 1999).

Measures used for the assessment of Self Injurious Behaviours

The Challenging Behaviour Questionnaire (CBQ; Hyman, Oliver & Hall, 2002)

The Challenging Behaviour Questionnaire was developed to assess the presence of four types of challenging behaviour in people with intellectual disability. These challenging behaviours include Self-Injurious Behaviour, physical aggression, destruction of property and stereotyped behaviour. The questionnaire asks parents/caregivers whether or not their child has displayed Self-Injurious Behaviours in the previous month week, year or day. Self-Injurious Behaviours include, head-banging, head-punching or slapping, removing hair, self-scratching, body hitting, eye-poking or pressing. Caregivers are also asked whether their child has shown physical aggression (punching, pushing, kicking, pulling hair, throwing objects, or grabbing other's clothing), property destruction (tearing or chewing own clothing, tearing newspapers, breaking windows or furniture, slamming doors, or spoiling a meal), and stereotypic behaviours (rocking, twiddling objects, patting or tapping part of the body, constant hand movements, or eye pressing).

The Motivation Assessment Scale (MAS; Durand & Crimmins, 1988)

The Motivation Assessment Scale explores problem behaviours by assessing the influence of social attention, tangibles, escape, and the sensory consequences on Self Injurious Behaviours. The Motivation Assessment Scale is a sixteen item questionnaire that assesses the functions or motivations of behaviour problems. The sixteen items are organized into four categories of reinforcement (attention, tangible, escape, and sensory). The Motivation Assessment Scale asks questions about the likelihood of a behaviour problem occurring in a variety of situations (e.g., when presented with difficult tasks). If one category (e.g., Escape) has clearly received the highest score, then it is assumed that this is the most important influence on the behaviour. Each category is given a mean

score (e.g., maximum mean score = 5.00). The highest mean score is considered to indicate that the category may be causing the problem behaviour to continue.

Participants

Characteristics of the Septo Optic Dysplasia group

Twenty-eight children were recruited, twelve were female and sixteen were male. The mean age in years of this group was 9.6 (SD: 34.5; range 4.2-16.0 years). Twelve participants were registered blind, of which three had some light perception, the reminder of children exhibited varying levels of visual impairments from mild to moderate. Three participants demonstrated a moderate to severe visual impairment, and in eight participants, visual function was categorised as normal to a mild impairment. Three children were partly able, one child needed partial help with walking and two used wheelchairs for mobility. Age Behaviour Composite Equivalence mean scores (as determined by the on the Vineland Adaptive Behaviour Scale: Sparrow, Balla & Ciccetti, 1987, see Methods section Measures) was 76.74 months (SD = 47.74) and Expressive Language Skills (as determined by the Vineland Adaptive Behaviour Scale: Sparrow *et al.*, 1984) was 97.88 months (SD= 54.88).

Optic Nerve Hypoplasia group

Fourteen children were recruited, six were female and eight were male. The mean age was 7.83 years (SD: 37.48; range: 4.8-12.2 years). The level of visual acuity ranged from, two children being registered blind, two children had a severe visual impairment, and the remainder exhibited vary levels of visual function from a mild to a moderate impairment. Two children were partly able, and both required partial help with walking but not wheelchair use. Age Behaviour Composite Equivalence mean scores (as determined by the on the Vineland Adaptive Behaviour Scale: Sparrow *et al.*, 1984) was

87.23 months (SD = 57. 51) and Expressive Language Skills (as determined by the Vineland Adaptive Behaviour Scale: Sparrow *et al.*, 1984) was 79.15 months (SD= 69.01).

Hypopituitarism group

Fourteen children were recruited, four were female and ten were male, and the mean age was 11.1 (SD: 46.1; Range: 5.2-16 years of age) and visual function was normal. Age Behaviour Composite Equivalence mean scores (as determined by the on the Vineland Adaptive Behaviour Scale: Sparrow *et al.*, 1984) was 89.88 months (SD = 52. 88) and Expressive Language Skills (as determined by the Vineland Adaptive Behaviour Scale: Sparrow *et al.*, 1984) was 133.86 months (SD= 53.54).

Individual participant characteristics for each syndrome are presented in table 6.4.1-6.4.3. Participant characteristics describe each child's chronological age, gender, level of visual loss (LP= light perception and AS = Astigmatism), Adaptive Behaviour Composite level and the reported presence (+) or absence (-) of Autism Spectrum Disorders according to the screening or diagnostic scales used to assess Autistic Spectrum Disorders.

Table 6.4.1: Child demographics for children with isolated cases of Hypopituitarism

Participant Number	Diagnosis	Chronological Age (months)	Gender	Vision	ABC Level	SCQ	GARS	ADOS	Clinician
1	Hypopituitarism	65	Male	Normal	Adequate	-	-	-	-
2	Hypopituitarism	170	Female	Normal	Moderately Low	-	-	-	-
3	Hypopituitarism	172	Female	Normal	Mild	-	-	-	-
4	Hypopituitarism	160	Female	Normal	Adequate	-	-	-	-
5	Hypopituitarism	109	Male	Normal	Moderately High	-	-	-	-
6	Hypopituitarism	166	Male	Normal	Adequate	-	-	-	-
7	Hypopituitarism	115	Male	Normal	Adequate	-	-	-	-
8	Hypopituitarism	79	Male	Normal	Adequate	-	-	-	-
9	Hypopituitarism	158	Male	Normal	Adequate	+	-	-	-
10	Hypopituitarism	72	Male	Normal	Moderately Low	-	-	-	-
11	Hypopituitarism	192	Male	Normal	Mild	-	-	-	-
12	Hypopituitarism	192	Male	Normal	Adequate	-	-	-	-
13	Hypopituitarism	78	Female	Normal	Adequate	-	-	-	-
14	Hypopituitarism	146	Male	Normal	High	-	-	-	-

Table 6.5.2: Child demographics for children with Optic Nerve Hypoplasia (ONH)

Participant Number	Diagnosis	Chronological Age (months)	Gender	Vision	ABC Ability	SCQ	GARS	ADOS	Clinician
15	ONH	72	Male	Severe	Mild	-	-	-	-
16	ONH	107	Male	Impaired	Severe	+	-	-	-
17	ONH	103	Male	Severe	Severe	-	-	-	-
18	ONH	125	Male	Profound	Moderate	+	-	+	+
***19**	**ONH**	**36**	**Male**	**Impaired**	**Moderately High**	-	-	-	-
***20**	**ONH**	**80**	**Male**	**Profound (LP)**	**Severe**	+	+	+	+
21	ONH	80	Female	Impaired (AS)	Adequate	-	-	-	-
***22**	**ONH**	**57**	**Female**	**Severe**	**Moderate**	+	+	+	-
23	ONH	192	Male	Severe	Profound	+	+	+	+
24	ONH	70	Female	Impaired	High	-	-	-	-
25	ONH	102	Female	Impaired	High	-	-	-	-
26	ONH	110	Female	Impaired	High	-	-	-	-
27	ONH	112	Male	Impaired	Adequate	-	-	-	-
28	ONH	69	Female	Impaired	Adequate	-	-	-	-

** and bold type face = children who completed the MAS and CBQ, which assessed self injurious behaviours*

Table 6.5.3: Child demographics for children with Septo Optic Dysplasia (SOD)

Participant Number	Diagnosis	Chronological Age (months)	Gender	Vision	ABC Ability	SCQ	GARS	ADOS	Clinician
***28**	**SOD**	**50**	**Male**	**Profound**	**Mild**	+	+	+	+
29	SOD	68	Male	Profound (LP)	Adequate	+	-	-	-
30	SOD	83	Female	Impaired	Adequate	-	-	-	-
31	SOD	84	Male	Impaired	Adequate	+	+	+	+
32	SOD	102	Female	Impaired	Adequate	+	-	+	+
***33**	**SOD**	**108**	**Female**	**Impaired**	**High**	+	+	+	-
34	SOD	110	Female	Severe	Mild	-	-	-	+
***35**	**SOD**	**120**	**Female**	**Severe (AS)**	**Mild**	+	+	+	+
36	SOD	121	Male	Severe (AS)	Mild	-	+	-	-
***37**	**SOD**	**132**	**Female**	**Impaired**	**Mild**	+	+	+	+
38	SOD	135	Male	Severe	Mild	-	-	+	-
39	SOD	145	Male	Severe	Mild	+	+	+	+
40	SOD	149	Male	Profound (LP)	Mild Deficit	+	+	-	-
41	SOD	156	Male	Profound	Moderately Low	+	+	+	-
42	SOD	84	Male	Profound	Moderately Low	+	-	-	-
43	SOD	162	Male	Severe (AS)	Moderately Low	+	-	+	-
44	SOD	89	Female	Profound	Moderate	-	-	-	-
45	SOD	90	Female	Impaired	Moderate	-	-	+	-
46	SOD	106	Female	Profound	Moderate	-	-	-	-
47	SOD	108	Male	Severe	Moderate	-	-	-	-
***48**	**SOD**	**101**	**Male**	**Profound**	**Moderate**	+	+	+	+
***49**	**SOD**	**151**	**Female**	**Profound**	**Moderate**	+	+	-	-
50	SOD	192	Female	Profound	Moderate	+	-	+	-
51	SOD	141	Female	Impaired	Profound	+	-	+	+

52	SOD	61	Male	Profound	Severe	-	-	-	-
***53**	**SOD**	**63**	**Male**	**Severe**	**Severe**	+	-	+	+
***54**	**SOD**	**89**	**Male**	**Impaired**	**Severe**	+	-	-	-
55	SOD	50	Male	Profound	Moderate	+	-	-	-
***56**	**SOD**	**48**	**Male**	**Profound**	**Mild**	+	+	+	+

** and bold type face = children who completed the MAS and CBQ, which assessed self injurious behaviours*

Procedure

Questionnaire packs were completed by parents/guardians of the children, which included the Social Communication Questionnaire and the Short Sensory Profile. Following the completion of the questionnaire pack, the Vineland Adaptive Behaviour Scale interview was completed over the telephone, or in person at the caregiver's home if they lived within the West Midlands area.

Children were identified as demonstrating self-injurious behaviours (SIB) through the parental reporting from the Social Communication Questionnaire (SCQ). From the SCQ, fourteen caregivers were identified and invited at a later date, to complete the CBQ which identified the types of SIB, and the Motivation Assessment scale (MAS) which explored the possible motivations behind observed Self Injurious Behaviours. Thirteen participants returned both the completed CBQ and MAS questionnaire.

Data analysis

Statistical analysis of measures for the assessment of restrictive, repetitive and stereotyped behaviours

Prior to analysis, all dependent measures for the assessment of Repetitive Behaviours met the assumptions of normality using the Shapiro-Wilk test. However, given the uneven group size data, group differences reported between children with isolated Hypopituitarism, Optic Nerve Hypoplasia and Septo- Optic Dysplasia and the presence of Repetitive and Stereotyped Behaviours on the Gilliam Autism Rating Scale, Social Communication Questionnaire and the Autism Diagnostic Observation Schedule were analysed using non-parametric Kruskall Wallis ANOVA, followed by post-hoc analyses. The percentage of children scoring above the cut-off point for the presence of Repetitive and Stereotyped Behaviours on the three scales used for the

assessment for Autistic Spectrum Disorders was compared through chi-square analysis. Pearson correlations were used to investigate the relationship between Repetitive and Stereotyped behaviours of the three scales, and the Total scores and the sub- domains, of the Autism Diagnostic Observation Schedule, the Social and Communication Questionnaire and the Gilliam Autism Rating Scale.

Within group characteristics of intellectual disability and language skills were explored in children with Optic Nerve Hypoplasia and Septo Optic Dysplasia using Pearson Correlations, Chi-squared test and independent samples t-test. Secondly, to investigate differences between Repetitive and Stereotyped behaviours in children with a Mild/Moderate, Severe/Moderate visual impairment, and total blindness, a series of one way ANOVAs were conducted, followed by ANCOVA, which controlled for intellectual disability. Lastly, to assess the relationship between sensory symptomatology and repetitive behaviours, chi squares tests of statistical association were carried out.

Statistical analysis of measures for the assessment of Sensory Processing Disorders

Exploratory analyses were initially conducted to establish whether data met parametric assumptions. Shapiro–Wilk W tests revealed statistically significant differences on the Short Sensory Profiles between children with isolated Hypopituitarism, Optic Nerve Hypoplasia and Septo Optic Dysplasia. Therefore, non-parametric analysis using the Kruskall-Wallis test was employed on the Sensory Total raw score, and sub-domains of Tactile, Taste/Smell, Movement, Auditory Sensitivity, Under-responsive/Seeks Sensation, Auditory Filtering and Low Energy raw scores. To explore the classification of sensory processing disorders, chi-square tests of association were

used between the child syndrome group and the Short Sensory Profile's classification of sensory impairments.

To assess the impact of autistic symptomatology, the Social Communication Questionnaire was used on children with Optic Nerve Hypoplasia and Septo Optic Dysplasia only. Firstly, Pearson correlations were used to look at the relationship between the SCQ and the Sensory Total Scores and Sensory sub-domain scores of the SSP.

The Short Sensory Profile of children with SOD/ONH were compared using t-tests according to whether children scored above, or below the cut-off point for Autistic Spectrum Disorders on the Social Communication Questionnaire Total Score, and sub domains of Communication, Social Interaction and Repetitive/Restrictive behaviours. To explore the classification of sensory processing disorders, Chi-square test of association were used between children who scored above, or below the cut-off point for Autistic Spectrum Disorders on the Social Communication Questionnaire and the Short Sensory Profile's classification of sensory impairments.

To assess the impact of intellectual disability and visual loss on children's Short Sensory Profiles, children with Septo Optic Dysplasia, Septo Optic Dysplasia and isolated Hypopituitarism were compared (n=56). Non-parametric analysis using the Kruskall-Wallis test was used to compare between the Adaptive Behaviour Composite of the VABS and the Sensory Total raw score, and the sub-domains; Tactile, Taste/Smell, Movement, Auditory Sensitivity, Under-responsive/Seeks Sensation, Auditory Filtering and Low Energy raw scores of the SSP. To explore the classification of sensory processing disorders, chi-square tests of association were used between children's level of intellectual disability and the Short Sensory Profile's classification of sensory impairments.

A one-way ANOVA was used to assess for differences between the level of visual impairment and the Total scores and the sub domains of the Short Sensory Profile. A one-way ANCOVA was also used to control for intellectual disability to explore the impact of visual loss on children's Short Sensory Profile Scores. In addition, a Chi-square analysis was conducted between the classification of sensory impairments according to the SSP and children's level of vision. Lastly, a binary logistic regression was conducted to assess which of these variables best predicted sensory impairments. A Bonfferonni correction was applied when multiple-comparisons were performed simultaneously to avoid type-I errors.

Statistical analysis of measures for the assessment of Self Injurious Behaviours

Initially, all children with Septo-Optic Dysplasia and Optic Nerve Hypoplasia were assessed for the presence or absence of SIB as identified through the SCQ. Due to the uneven sample size, statistical comparison using Mann-Whitney- *U* tests between children for the presence (+) or absence (-) of Self Injurious Behaviours and the impact of intellectual disability using the Adaptive Behaviour Composite mean age equivalence scores from the Vineland Adaptive Behaviour Scale were carried out.

Furthermore, using Chi-Square test of association, differences between children's level of visual loss, autistic phenomenology and the reporting of Self-Injurious Behaviours was compared. Statistical comparison using X^2 or Mann-Whitney- *U* statistical tests, were also used to explore for differences between the Domains of Communication, Social Interaction and Repetitive behaviours of the SCQ and Self Injurious Behaviours.

For the thirteen children who had completed with CBQ and MAS, the percentage occurrence of the types of Self Injurious Behaviours and a description of each child and

their characteristics was reported. Using a Chi-square test of association the difference between visual loss, autistic disorders and Self Injurious Behaviours was analysed. Pearson correlations were used to explore the relationship between intellectual disability and Self Injurious Behaviours.

6.5 Results

6.5 .1 Relationship between Repetitive Behaviours and syndrome group

Group differences were reported between children with isolated Hypopituitarism, Optic Nerve Hypoplasia and Septo- Optic Dysplasia for the presence of Repetitive and Stereotyped behaviours on the Gilliam Autism Rating Scale, Social Communication Questionnaire and the Autism Diagnostic Observation Schedule. Table 6.5.1 summarises these findings.

Table 6.5.1: Mean rank scores of children's Repetitive and Stereotyped Behaviours on the GARS, SCQ and ADOS for the assessment for Autistic Spectrum Disorders

Repetitive Behaviours	Diagnosis	Mean Rank	X^2	df	*p*-value
GARS	Hypopituitarism	131.55	103.82	2	.00*
	Optic Nerve Hypoplasia	382.19			
	Septo Optic Dysplasia	390.27			
SCQ	Hypopituitarism	165.87	132.73	2	.00*
	Optic Nerve Hypoplasia	285.73			
	Septo Optic Dysplasia	421.45			
ADOS	Hypopituitarism	250.86	24.98	2	.00*
	Optic Nerve Hypoplasia	343.20			
	Septo Optic Dysplasia	374.58			

**Statistical significance at 0.01*

To assess where the difference lay between groups, post-hoc analyses were performed. T-test and Mann-Whitney U tests were used and significant differences were reported between children with Hypopituitarism and Optic Nerve Hypoplasia ($t(28) = 3.16$; $p \leq 0.05$ and between children with Septo Optic Dysplasia and Hypopituitarism ($Z = -3.80$; $p \leq 0.01$). However, no significant differences were reported between children with Septo Optic Dysplasia and Optic Nerve Hypoplasia ($z = -.39$; $p \geq 0.05$).

Of the fifty-six children who were evaluated on all three measures for Autistic Spectrum Disorders, children who received a diagnosis of Optic Nerve Hypoplasia or Septo-Optic Hypoplasia showed the greatest percentage of Repetitive and Stereotyped behaviours. Table 6.5.2 shows the percentage of children with isolated Hypopituitarism, Optic Nerve Hypoplasia and Septo Optic Dysplasia who scored above the cut-off point for the presence of Repetitive and Stereotyped Behaviours on the Social Communication Questionnaire and the Gillian Autism Rating Scale Domain.

As the Autism Diagnostic Observation Schedule does not utilise Stereotyped Behaviorsand Restrictive Interests for the classification of Autism Spectrum Disorders, no cut-off point was available, instead the percentage of children who showed the presence of Repetitive behaviours during the Autism Diagnostic Observation Schedule was compared between syndrome groups.

Table 6.5.2: Percentage of children scoring above the cut-off point for the presence of Repetitive and Stereotyped Behaviours on the three scales for the assessment for Autistic Spectrum Disorders.

Diagnosis	SCQ	ADOS	GARS
	Repetitive Behaviours Domains		
Hypopituitarism total %	7.14	0.00	7.14
Optic Nerve Hypoplasia total %	46.60	42.86	46.60
Septo Optic Dysplasia total %	57.71	53.57	39.29
Total % of all participants	42.10	45.23	33.33

As only one child with Isolated Hypopituitarism met the cut-off point for Repetitive Behaviours on the Social Communication Questionnaire and Gilliam Autism Rating Scale, children with Septo-Optic Dysplasia and Optic Nerve Hypoplasia only were examined, for statistical analysis. Furthermore, looking at the means of children with Septo-Optic Dysplasia and Optic Nerve Hypoplasia in table 6.5.3 there was little difference between the two groups.

Table 6.5.3: Mean score of the repetitive Behaviour Domain sub-scales of the three assessments in children with Septo-Optic Dysplasia and Optic Nerve Hypoplasia

Repetitive Behaviour Domain	Diagnosis	Mean	SD
SCQ	ONH	2.90	2.29
	SOD	3.89	3.06
GARS	ONH	11.92	9.93
	SOD	11.93	8.48
ADOS	ONH	1.46	2.33
	SOD	2.11	2.59

At least 81% (n=18) of children who scored above the cut –off point for Autistic Spectrum Disorders on the Social Communication Questionnaire, also scored above the cut-off point for on the domain of Stereotyped Behaviours of the Social Communication Questionnaire. The relationship between scoring above the cut-off point for Autism Spectrum Disorders and meeting the cut-off point for Stereotyped/ Repetitive Behaviours on the Social Communication Questionnaire was significant (X^2 (2) = 16.85, p <.001).

In addition, 66% (n=12) of children who scored above the cut-off point for Autistic Spectrum Disorders on the Gilliam Autism Rating Scale, also scored above the cut-off point for the presence on the Stereotyped Behaviours domain of the Questionnaire. The difference between scoring above the cut-off point for Autism Spectrum Disorders and meeting the cut-off point for Stereotyped/ Repetitive Behaviours on the Gilliam Autism Rating Scale was significant (X^2 (2) = 14.3, p <.001).

Of the 77% (n=14) of children who scored above the cut –off point for Autistic Spectrum Disorders on the Autism Diagnostic Observation Schedule, also showed the presence of Stereotyped Behaviours during the ADOS assessment. The difference between scoring above the cut-off point for Autism Spectrum Disorders and scoring on the Stereotyped/ Repetitive Behaviours domain of the Autism Diagnostic Observation Schedule was significant (X^2 (2) = 10.10, p <002).

Interestingly, of the thirteen children who received a diagnosis from a Clinician, 66% exhibited stereotyped behaviours and Restrictive Interests during the Autism Diagnostic Observation Schedule, 54 % scored above the cut off point for Stereotyped Behaviours on the Social Communication Questionnaire and 57% scored above the cut-off point for Stereotyped Behaviours on the Gilliam Autism Rating Scale. The relationship between a diagnosis of Autism from a Clinician and scoring above the cut-off point for Repetitive behaviours was significant between the Social and Communication

Questionnaire (X^2 (2) = 18.11, p <001) and the Autism Diagnostic Observation Schedule (X^2 (2) = 10.10, p <002 but not the Gilliam Autism Rating Scale (X^2 (2) = 5.96, p >.31).

To investigate the relationship between Total scores and the sub domains of Communication and Social Interaction, on the Autism Diagnostic Observation Schedule, the Social and Communication Questionnaire and the Gilliam Autism Rating Scale, Pearson correlations were conducted between the Total score, Communication and Social Interaction sub-domains scores, and the sub-domain of Repetitive and Stereotyped behaviours of the three scales. This is summarised in table 6.5.4.

Table 6.5.4: the relationship between Total and the sub domains of Communication and Social Interaction on the Autism Diagnostic Observation Schedule, the Social and Communication Questionnaire and the Gilliam Autism Rating Scale

Overall Score/ Sub-Domains	Repetitive/ Stereotyped Domains		
	GARS	ADOS	SCQ
Social interaction	.60**	.77*	.07
Communication	.72**	.69*	.422**
Total	.67**	.78**	.62**

** ≤ 0.01

Pearson correlation coefficients between; 0 to 0.2 are considered weak, 0.3 to 0.6 to moderate and 0.7 to 1.0 strong. Significant strong positive correlations were demonstrated between repetitive and stereotyped behaviours and the Total scores of the three scales. Statistically, significant strong positive correlations were demonstrated between repetitive and stereotyped behaviours and the Social Interaction domain of the Autism Diagnostic Observation Schedule and the Gilliam Autism Rating Scale but not the Total score of the Social and Communication Questionnaire. The relationship between

Repetitive and Stereotyped Behaviours and Communication was reported as statistically, significantly strong for the Social Interaction domain of the Autism Diagnostic Observation Schedule and the Gilliam Autism Rating Scale, but only moderate for the Social and Communication Questionnaire.

Comparison of Participant characteristics and Repetitive and Stereotyped Behaviours

The within group characteristics of children with Optic Nerve Hypoplasia and Septo Optic Dysplasia were compared. Specifically, the effect of gender, chronological age, level of ability, receptive and expressive language skills was investigated.

To investigate the relationship between chronological age, the domain and sub domains of the Vineland Adaptive Behaviour Scale and Repetitive and Stereotyped Behaviours sub-domain raw scores of the Autism Diagnostic Observation Schedule, the Social Communication Questionnaire, and the Gilliam Autism Rating Scale were looked at using Pearson correlations, table 6. 5.5 summarises these analyses.

Table 6.5.5: The relationship between chronological age, the domain and sub domains of the Vineland Adaptive Behaviour Scale and Repetitive and Stereotyped Behaviours sub-domain raw scores of the Autistic Spectrum assessments

Chronological Age and Adaptive Behaviour / VABS – Sub Domains	Repetitive/ Stereotyped Behaviours Domain		
	GARS	ADOS-G	SCQ
Chronological Age	.31	.15	.23
ABC Age Equivalence	-.27	-.42**	-.38*
Receptive Language	-.30	-.30	-.17
Expressive Language	-.11	-.28	-.07
Communication	-.03	-.12	-.17
Socialisation Skills	.19	-.09	.09
Daily Living Skills	.11	.04	.10

** $p < 0.01$; $p < 0.05$

Statistically, moderate negative significant correlations were reported between the Adaptive Behaviour Composite Mean Age Equivalence and the Repetitive and Stereotyped Behaviours domain raw scores of the Autism Diagnostic Observation Schedule and the Social and Communication Questionnaire, showing that lower scores on the ABC (i.e. higher degree of intellectual disability) was related to significantly higher Repetitive and Stereotyped Behaviours domain raw scores on the assessments (i.e. greater incidence of repetitive behaviours).

Comparison of intellectual disability and Repetitive and Stereotyped behaviours in children with isolated Hypopituitarism, Septo Optic Dysplasia and Optic Nerve Hypoplasia

Looking at the group as a whole (n=56), independent samples t-tests were used. No statistically significant differences were reported between children who scored above the cut off point (mean 95.51, SD = 44.06) and children who scored below the cut-off point (85.68, SD 46.68) for Repetitive Behaviours on the Social Communication Questionnaire (t (1, 55) = .80; $p > 0.05$) or the Gilliam Autism Rating Scale (t (1, 55) = .68; $p > 0.05$).

When children with Septo Optic Dysplasia and Optic Nerve Hypoplasia, were grouped according to ability, as either, above/average (no disability group), mild/moderate and severe/profound intellectual disability and compared on the Repetitive and Stereotyped Behaviours domain raw scores on the assessments, no statistical differences were reported between groups on the Social Communication Questionnaire (X^2 (42) = .89; $p > .01$), the Gilliam Autism Rating Scale (X^2 (42) = .92; $p > .01$) and the Autism Diagnostic Observation Schedule (X^2 (42) = 4.7; $p > .01$).

Comparison of Visual Acuity and Repetitive and Stereotyped behaviours in children with Septo Optic Dysplasia and Optic Nerve Hypoplasia

To investigate group differences between Repetitive and Stereotyped behaviour in children with a Mild/Moderate, Severe/Moderate visual impairment, and total blindness, a series of One Way ANOVAs were conducted. Table 6.5.6 summarises the mean scores on the sub domains of Repetitive behaviours of the Social Communication Questionnaire, the Gilliam Autism Rating Scale and the Autism Diagnostic Observation Schedule. No statistically, significant differences were reported between level of vision and severity of repetitive behaviours.

Table 6.5.6: The mean repetitive behaviour scores on the SCQ, ADOS and GARS according to level of vision

Sub- domain Repetitive/ Stereotyped Behaviours		Level of Vision					
		Mild/Moderate (n=15)	Moderate/ Severe(n=13)	Blind/Light Perception (n=14)	One Way ANOVA F	df	*p-value*
SCQ	Mean(SD)	3.79 (3.09)	3.62 (3.10)	3.36 (2.53)	0.90	2, 39	.48
GARS	Mean(SD)	9.64 (7.87)	12.77 (7.87)	14.00(9.13)	0.08	2, 39	.93
ADOS	Mean(SD)	1.43(1.79)	2.08(3.37)	2.21(2.40)	3.80	2, 39	.69

When the Adaptive Behaviour Composite age equivalence was used as a covariate, no statistical differences were reported (F (2, 39) = 0.90; p >.01) between the Repetitive Behaviour domain of the Gilliam Autism Rating Scale and children's level of vision. In addition, when repeating this analysis, for the SCQ Repetitive Behaviours

domain, no statistical differences were reported between children's level of vision ($F(2, 39) = 3.64$; $p > .01$).

Comparison of Sensory Impairments and Repetitive and Stereotyped behaviours in children with Septo Optic Dysplasia and Optic Nerve Hypoplasia

Lastly, to assess the difference between sensory symptomatology and repetitive behaviours, chi squares test analysis showed significant statistical difference between sensory classifications using the Short Sensory Profile and scoring above the cut-off point for Repetitive Behaviours on the Social Communication Questionnaire, and the Gilliam Autism Rating Scale. Table 6.5.7 summarises the findings.

Table 6.5.7: Sensory classifications using the short sensory profile and scoring above the cut-off point for Repetitive Behaviours

Repetitive/Stereotyped Behaviour Domain		Sensory Classification			X^2	df	*p-value*
		Typical	Probable	Definite			
SCQ	-	35.% (7)	25.% (5)	40.% (8)	5.92	2	.05
	+	10% (2)	14.% (3)	76 % (16)			
GARS	-	35% (7)	25% (5)	40% (8)	9.19	2	.01
	+	22% (2)	14% (3)	76% (16)			
*ADOS		16.44(9)	19.88(8)	22.30 (23)	1.90	2	.39

+ = scoring above the cut off point , - = scoring below the cut point for Autism Spectrum Disorders.

* *percentage of participants showing repetitive behaviours and T-test analysis results*

Syndrome group differences in the parental report of Sensory Symptomatology in children with isolated Hypopituitarism, Optic Nerve Hypoplasia and Septo Optic Dysplasia.

Differences between child syndrome group mean rank scores and the statistical analysis of the Short Sensory Profile (SSP) are summarised in Table 6.6.1. The analysis found that children with isolated Hypopituitarism had higher mean rank scores, indicating a fewer number of sensory impairments, compared to children with Optic Nerve Hypoplasia and Septo Optic Dysplasia. The raw scores of the SSP show that children with Optic Nerve Hypoplasia and Septo Optic Dysplasia scored similarly.

Table 6.6.1: The Mean rank scores and statistical analysis of the of Short Sensory Profiles (SPP) Total and Sub domain scores according to child syndrome group

Short Sensory Profile (SPP)		Hypopit-uitarism	Optic Nerve Hypoplasia	Septo Optic Dysplasia	X^2	*df*	*P-value*
Tactile Sensitivity	Mean	31.00	29.07	26.61	7.23	2	.27
	SD	8.60	4.34	7.34			
Taste and Smell	Mean	18.29	13.42	13.92	5.01	2	.08
	SD	5.61	5.92	5.51			
Movement Sensitivity	Mean	16.71	13.07	12.90	3.38	2	.18
	SD	8.64	2.92	3.35			
Under Responsive/ Seeks sensation	Mean	27.50	20.71	21.07	6.52	2	.04
	SD	7.81	7.508	8.17			
Auditory Filtering	Mean	24.14	18.07	19.18	7.02	2	.30
	SD	5.78	5.48	6.40			
Low Energy & Weak	Mean	26.71	21.07	19.00	9.96	2	.00**
	SD	5.14	6.09	8.17			
Auditory Sensitivity	Mean	9.00	6.07	5.75	15.60	2	.00**
	SD	2.22	2.56	2.53			
Total Sensory Score	**Mean**	**152.21**	**121.79**	**121.79**	**15.16**	**2**	**.00****
	SD	**15.77**	**17.70**	**26.73**			

*Bonfferonni correction at p<0.0125**; p< 0.01**.*

Table 6.6.1 also shows that statistically significant differences were reported between syndrome groups, and the Total Sensory Score, the sensory sub-domains of Low Energy/Weak, and Auditory Sensitivity of the Short Sensory Profile.

As the Kruskall -Wallis analysis does not employ post-hoc tests to investigate where statistical significance is positioned between syndrome groups, children with isolated Hypopituitarism, Optic Nerve Hypoplasia and Septo Optic Dysplasia were compared using pair-wise comparisons.

Analysis of the mean scores, using t tests between children with Optic Nerve Hypoplasia and isolated Hypopituitarism, revealed statistically significant differences between Sensory Score Total score, ($t(28) = 4.89, p < 0.01$), the Sensory sub-domains of, Under Responsive/Seeking Sensation ($t(28) = 2.34, p < 0.05$), Auditory Filtering ($t(28) = 2.85, p < 0.01$), Low Energy ($t(28) = 2.65, p < 0.05$), Auditory Sensitivity ($t(28) = 3.24, p < 0.01$) and Taste and Smell ($t(28) = 2.23), p < 0.05$), but no statistically significant differences were reported between syndrome groups for the Movement Sensitivity ($t(28) = 1.49, p > .05$) or Tactile Sensitivity sub-domains ($t(28) = 0.75\ p > .05$).

Secondly, a comparison between the mean rank scores of children with isolated Hypopituitarism and Septo Optic Dysplasia using Mann-Whitney *U*, tests revealed statistically significant differences between the Sensory Total Score, ($U(42) = 68.50, p < 0.01$), the sub domains of Auditory Sensitivity ($U(42) = 54.50, p < 0.05$), Low Energy ($U(42) = 84.50, p < 0.01$), Auditory Filtering ($U(42) = 113.00, p < 0.05$), Under Responsive/ Seeking Sensation ($U(42) = 109.00, p < 0.05$), Taste and Smell ($U(42) = 119.00, p < 0.05$), and Tactile Sensitivity ($U(42) = 111.00, p < 0.05$). However, no statistically significant differences were found between syndrome groups and the Movement Sensitivity sub-domain ($U(42) = 146.00, p > 0.05$).

Lastly, a comparison between children with Septo Optic Dysplasia and Optic Nerve Hypoplasia, using Mann-Whitney *U* analysis revealed no statistically significant differences on the mean rank scores of the Sensory Total Score, (U (42) = 195.50, $p >$ 0.05); Auditory Sensitivity (U (42) = 184.50, $p > 0.05$), Low Energy (U (42) = 160.00, $p > 0.05$), Auditory Filtering (U (42) = 176.00, $p > 0.05$), Under Responsive/ Seeking Sensation (U (42) = 196.50, $p > 0.05$), Taste and Smell (U (42) = 184.00, $p > 0.05$ and Tactile Sensitivity (U (42) = 170.50, $p > 0.05$), and Movement Sensitivity, (U (42) = 173.50, $p > 0.05$).

The post-hoc analysis indicates that within group characteristics of intellectual disability and visual impairment, which are common to both children with Optic Nerve Hypoplasia and Septo-Optic Dysplasia, differentiate sensory scoring profiles (except Movement Sensitivity) from that of children with isolated Hypopituitarism.

The Classification of Sensory Difficulties by the Short Sensory Profile

Children with Hypopituitarism showed a fewer number of sensory impairments in comparison to children with Septo Optic Dysplasia and Optic Nerve Hypoplasia. At least, 71.4% (n= 10) of children with isolated Hypopituitarism had a Typical Sensory Profile, 21.4% (n= 3) showed Probable Differences, and only 7.1% (n= 1) were classified as having a Definite Difference in their Short Sensory Profile score. However, only 15.4% (n=2) children with Optic Nerve Hypoplasia were classified as having a Typical Sensory Profile, 30.8% (n= 4) demonstrated Probable Differences, and 53.8% (n =8) showed Definite Differences in their Short Sensory Profile scores. The percentage of children with Septo Optic Dysplasia who were classified as Typical in their Short Sensory Profile was, 25% (n=7), 14.3% (n=4) showed Probable Differences, and 60.7% (n=17) showed Definite Differences in their Short Sensory Profile. Thus, the difference between

the three syndrome groups, and their Sensory Profile Classification was statistically significantly different (X^2 (3) = 15.02, $p < 0.05$).

The Relationship between the Sensory Symptoms and Autistic Spectrum Disorders in children with Septo-Optic Dysplasia and Optic Nerve Hypoplasia.

As no children with isolated Hypopituitarism exhibited autistic phenomenology, the following section will explore the impact of autistic symptomatology using the Social Communication Questionnaire (SCQ Lord, Rutter & Pickles, 1999) on children with Optic Nerve Hypoplasia and Septo Optic Dysplasia sensory profiles.

Using the Short Sensory Profile raw scores, Pearson correlations were used on the Social Communication Questionnaire raw scores and the Sensory Total and Sensory sub-domain raw scores. Strong negative correlation was reported between the Stereotyped Behaviours of the Social Communication Questionnaire the sub-domain and the Tactile Sensitivity sub domain of the Short Sensory Profile. Table 6.6.2, reported a strong statistical significant negative correlation between the Social Interaction domain of the SCQ and the Tactile Sensitivity domain of the SSP.

Table 6.6.2: Correlations between the Short Sensory Profile subscales and SCQ sub domains in children with Septo-Optic Dysplasia and Optic Nerve Hypoplasia

N= 42	SCQ Raw Scores- Total and Sub Domain			
Short Sensory Profile Domains and Total Score	Total Score	Social Interaction	Communication	Stereotyped Behaviours
Under Responsive/ Seeks Sensation	.227	-.335*	-.269	-.296
Auditory Sensitivity	.257	-.146	-.076	-.239
Low Energy	.059	-.262	-.318*	-.177
Auditory Sensitivity	-.094	-.225	-.362*	**-.343***
Tactile Sensitivity	.133	-.463**	-.346**	**-.527****
Taste and Smell Sensitivity	.044	-.110	-.017	-.386**
Movement Sensitivity	-.12	-.060	-.208	-.142
Sensory Total Score	-.13	-.307*	-.294	-.468**

*$p<0.05$** $p<$ *0.01; strong correlations are identified in bold typeface.*

The difference between the Sensory Symptomology in children with Septo-Optic Dysplasia and Optic Nerve Hypoplasia who were suspected of ASD.

The Short Sensory Profiles of children with SOD/ONH, who scored above, or below the cut-off point for Autistic Spectrum Disorders according to the Social Communication Questionnaire Total Score, and sub-domains of Communication, Social Interaction and Repetitive/Restrictive was compared.

Tables 6.6.3 summarises the mean and statistical association between syndrome groups and SCQ using chi-squared tests of association. Appendix Nine summarises table 6.6.3.1, 6.6.3.2 and 6.6.3.3, which assess the Short Sensory profile raw scores and the

sub-domains of Communication, Social Interaction and Repetitive/Restrictive Behaviours.

Table 6.6.3: Sensory Symptoms within group of children with ONH/SOD and with (-) and without (+) ASD according to SCQ total Score.

Sensory Domain	SCQ Total Score	N	Mean	SD	*t*	*N*	*p-value*
Tactile Sensitivity	-	18	27.16	6.76	-.241	42	.811
	+	24	27.65	6.49			
Taste and Smell Sensitivity	-	18	13.63	6.36	-.136	42	.893
	+	24	13.87	4.99			
Movement Sensitivity	-	18	13.00	3.11	.087	42	.931
	+	24	12.91	3.30			
Under responsive Seeks Sensation	-	18	20.53	8.15	-.316	42	.754
	+	24	21.30	7.78			
Auditory Filtering	-	18	17.58	5.73	-1.20	42	.237
	+	24	19.83	6.27			
Low Energy	-	18	19.95	7.81	.198	42	.844
	+	24	19.48	7.46			
Auditory Sensitivity	-	18	6.58	2.34	1.73	42	.091
	+	24	5.26	2.54			
Total Sensory Score	-	18	121.00	23.99	-.145	42	.885
	+	24	122.09	24.30			

(+) scoring above the cut-off for ASD, (-) scoring below the cut-off for ASD.

Overall, there were no reported differences between children with, or without Autistic Spectrum Disorders on their Total Sensory Scores. This suggests that autistic symptomatology did not contribute to differential reporting of sensory impairments between groups. However, table 6.6.3.1, 6.6.3.2 and 6.6.3.3 showed that statistically significant differences were reported between, scoring above or below the cut-off point on the Reciprocal Interaction domain and Repetitive Behaviours domain of the Social Communication Questionnaire and the sub-domain of Taste and Smell Sensitivity and Auditory Sensitivity of the Short Sensory Profile. Looking at the classification of Sensory impairments according to the Short Sensory Profile, a statistically significant difference

was reported between the classifications of Sensory differences and scoring above or below the cut-off point for Autistic Spectrum Disorders on the Social Communication Questionnaire. Table 6.6.4 summarises the analysis.

Table 6.6.4: differences between the classifications of sensory differences by the SSP, according to Autistic Spectrum Disorders as measured by the SCQ

Social Communication Questionnaire		Sensory Classification (Short Sensory Profile) (n=55)					
		Typical Performance	Probable Difference	Definite Difference	X^2	*df*	*p - value*
Stereotyped Behaviours	-	51.5% (n=17)	24.2% (n=8)	24.2% (n=8)			
	+	9.1% (n=2)	13.6% (n=3)	77.3% (n=17)	15.79	2	.00**
Communication	-	48.5% (n=16)	18.2% (n=6)	33.3% (n=11)			
	+	13.6% (n=3)	22.7% (n=5)	63.6% (n=14)	7.44	2	.02*
Reciprocal Interaction	-	51.4% (n=18)	14.3% (n=5)	34.3% (n=12)			
	+	5.0% (n=1)	30.0% (n=6)	64.0% (n=13)	12.12	2	.00**
Total SCQ	-	50.0% (n=16)	18.8% (n=6)	31.3% (n=10)			
	+	13.6% (n=3)	22.7% (n=5)	63.6% (n=14)	8.08	2	.02*

(+) scoring above the cut-off for ASD, (-) scoring below the cut-off for ASD;**

Bonferroni correction was applied, significance was at 0.0125;*significance at 0.05*.

Relationship between domain scores of Sensory Symptoms and level of Intellectual Disability

The following section used all child syndrome groups (n=56), to assess the impact of intellectual disability on children's Short Sensory Profiles. Table 6.6.5 summarises that the sub domains of the Short Sensory Profile raw scores did not differ according to intellectual disability. However, using the less conservative significance level, differences were reported between the SSP total score and degree of intellectual disability.

6.6.5. Differences be between the raw scores of the total and sub-domain scores of Short Sensory Profile according to the level of intellectual ability/disability

Short Sensory Profile Total and Domain Scores		*Degree of Intellectual Ability/Disability				X^2	*df*	*p-value*
		Above/ Average (n=20)	Mild (n=14)	Moderate (n=14)	Severe/ Profound (n=8)			
Tactile Sensitivity	Mean Rank	37.10	25.25	24.04	20.50	9.25	3	.026
Taste and Smell	Mean Rank	33.48	23.86	27.07	26.69	3.39	3	.342
Movement Sensitivity	Mean Rank	28.58	29.50	29.54	24.75	6.38	3	.889
Under-responsive Seeks Sensation	Mean Rank	34.90	27.07	26.43	18.63	6.38	3	.094
Auditory Filtering	Mean Rank	34.35	27.07	22.11	27.56	4.89	3	.181
Low Energy	Mean Rank	35.15	28.82	21.57	23.44	6.74	3	.081
Auditory Sensitivity	Mean Rank	35.95	25.32	20.79	28.94	8.03	3	.045
Sensory Total Score	Mean Rank	37.55	26.07	21.82	21.81	10.19	3	.017**

level of intellectual disability/ability was derived from the Adaptive Behaviour Composite (ABC) of the Vineland Adaptive Behaviour Scale. * Bonfferonni correction was applied, significance was at 0.00625; significance achieved at the less conservative vale of 0.05.*

However, a significant statistical difference was reported between children's level of intellectual disability and their classification of sensory impairments according to the Short Sensory Profile. Table 6.6.6 summarises these findings and also shows that more children with a moderate to profound level of intellectual disability showed Definite Differences in the Sensory Profiles when compared to children with average or above average levels of adaptive ability.

6.6.6 Differences between the classification of sensory impairments according to the Short Sensory Profile and children's the level of intellectual ability/ disability.

*Level of Intellectual Disability (ABC)	Sensory Classification according to the Short Sensory Profile					
	Typical Performance	Probable Difference	Definite Difference	X^2	*df*	*p-Value*
Above/Average (n =20)	60% (n=12)	20% (n=4)	14.3% (n=2)	15.35	3	.018
Mild (n =14)	28.6% (n=4)	14.3% (n=2)	14.3% (n=2)			
Moderate (n =12)	14.3% (n=2)	14.3% (n=2)	71.4% (n=10)			
Severe/ Profound (n= 8)	0%	25.0% (n=2)	75.0% (n=6)			

**level of intellectual disability/ability was derived from the Adaptive Behaviour Composite (ABC) of the Vineland Adaptive Behaviour Scale.*

The Relationship between the Short Sensory Profile (SSP) Domain and Total Score and level of Visual function

Table 6.6.7, summarises that the Total scores, the sub domains of; Under-responsive/Seeks Sensation and Auditory Sensitivity of the Short Sensory Profile differed significantly according to the level of visual impairment.

Table 6.6.7: Differences between raw domain scores of the Short Sensory Profile according to children's level of Visual function

Short Sensory Profile (SSP) Domain and Total Score		Normal (n=14)	Impaired (n=16)	Severe (n=12)	Profound Blind (n=14)	F	*df*	*p-value*
Tactile Sensitivity	M	31.00	30.13	26.42	25.21	2.28	3,52	.090
	SD	8.60	4.72	7.30	6.10			
Taste and Smell	M	18.29	14.56	13.41	13.14	2.41	3,52	.078
	SD	5.61	5.05	6.01	6.09			
Movement Sensitivity	M	16.71	13.31	12.25	13.14	1.98	3,52	.129
	SD	8.64	3.32	3.33	3.03			
Under responsive/ Seeks Sensation	M	27.50	25.31	14.83	21.21	8.12	3,52	.000*
	SD	7.81	6.916	5.22	7.67			
Auditory Sensitivity	M	24.14	20.38	15.58	19.79	4.68	3,52	.006
	SD	5.78	5.88	6.78	4.87			
Low Energy	M	26.71	22.56	16.50	19.14	5.58	3,52	.002
	SD	5.14	6.47	6.49	8.67			
Auditory Sensitivity	M	9.00	6.25	4.92	6.21	6.67	3,52	.001*
	SD	2.29	2.46	2.61	2.46			
Sensory Total Score	**M**	**152.21**	**132.00**	**104.42**	**124.43**	**12.44**	**3,52**	**.000***
	SD	**15.77**	**19.52**	**25.03**	**20.34**			

*** Bonfferonni correction was applied, significance was at 0.00625;**

Furthermore, a one way between analyses of covariance was conducted to compare the Short Sensory Total Score and children's level of visual impairment, when using the level of intellectual disability according to the Adaptive Behaviour Composite (ABC) of the Vineland Adaptive Behaviour Scale as a covariate in the analysis. After adjusting for intellectual disability, a significant difference was still reported (F (3, 53) = 11.92, p = 0.00, partial eta squared = .427. There was a weak relationship between the

Total Sensory Score and intellectual disability, as indicated by a partial eta squared value of 0.2.

In addition, **a** Chi-square analysis was conducted which reported statistically significant differences between the reporting of sensory impairments and children's level of vision. Table 6.6.8 also summarises that children with impaired vision and complete visual loss showed more definite differences in their sensory symptoms according to the Short Sensory Profile.

6.6.8: Differences between the classification of sensory impairments according to the Short Sensory Profile and children's the level of visual function

	Sensory Classification according to the Short Sensory Profile					
Level of Visual Acuity	Typical Performance	Probable Difference	Definite Difference	X^2	*df*	*p-Value*
Normal Vision (n =14)	71.4% (n=10)	21.4% (n=3)	7.1% (n=1)	20.72	3	.002
Impaired Vision (n =16)	31.3% (n=5)	25.0% (n=4)	43.8% (n=7)			
Severe Visual Impairment (n =12)	8.3% (n=1)	8.3% (n=1)	83.3% (n=10)			
Profound/Blind (n= 14)	14.3% (n=2)	14.3% (2)	71.4% (10)			

To confirm that the level of visual impairment was the best predictor of sensory impairments, a binary logistic regression was conducted to assess which of these variables best predicted sensory impairments. The categorical dependent variable was scoring above the cut-off point between typical performance and probable/definite differences on the Short Sensory Profile. The two continuous independent variables were: the mean-age

equivalence scores of the Adaptive Behaviour Composite to assess degree of intellectual disability and level of visual impairment as the categorical independent variable.

The best predictor of scoring above the cut- off point for impaired sensory symptoms was level of visual function, Under the Multiple Regression Enter method, a significant model emerged ($F_{1,54} = 4.44$, $p < 0.05$). Adjusted R square 11.3= Significant variables are summarised in table 6.6.9.

Table 6.6.9: A binary logistic regression to assess which best predicted sensory impairments in children with Septo-Optic Dysplasia, Optic Nerve Hypoplasia and isolated Hypopituitarism.

Predictor Variable	Beta	*p-value*
Level of Vision	-13.46	.01**
Adaptive Behaviour Composite Age Equivalence level in Months (VABS)	-.08	.83

The occurrence of Self Injurious Behaviours in Children with Septo Optic Dysplasia and Optic Nerve Hypoplasia.

According to the SCQ the prevalence of Self Injurious Behaviours in the overall cohort (n=56) was 33% (14). Three children with Optic Nerve Hypoplasia (14%) and ten children with Septo Optic Dysplasia (39%) reported Self Injurious Behaviours.

The relationship between Intellectual Disability, Adaptive Behaviours and Self Injurious Behaviours

Children, who presented with Self Injurious Behaviours according to the SCQ, showed greater degrees of intellectual disability. The Adaptive Behaviour Composite mean age equivalence score reported statistically significant differences between the presence and absence of Self Injurious Behaviours, indicating that Self Injurious Behaviours were dependent on children's overall adaptive behaviour functions. However, at domain levels no statistically significantly differences were reported, although the mean age equivalence scores were lower for children who presented with Self Injurious Behaviours than for children who did not display Self Injurious Behaviours. Table 6.7.1 summarises these findings.

Table 6.7.1: Mean Standard Deviation (SD) and statistical analysis between the VABS Total and Domain levels according to the Presence or absence of Self Injurious Behaviours according to the SCQ in children with SOD/ONH

VABS Sub – Domain Age Equivalence in Months	Presence (+) or Absence (-) of SIB	N	Mean	SD	*U*	*df*	p-value
Communication	- SIB	28	96.79	53.43	151.00	2	.70
	+ SIB	14	87.80	4.80			
Expressive Language	- SIB	28	88.01	60.04	168.00	2	.06
	+ SIB	14	60.00	56.89			
Receptive Language	- SIB	28	57.58	34.21	160.00	2	.68
	+ SIB	14	30.38	24.74			
Daily- Living Skills	- SIB	28	54.81	44.47	115.00	2	.08
	+ SIB	14	63.85	30.17			
Socialisation Skills	- SIB	28	65.23	49.39	124.50	2	.14
	+ SIB	14	79.15	33.20			
ABC	- SIB	28	77.92	33.00	92.00	2	.007*
	+ SIB	14	47.36	22.34			

**Bonfferonni correction at 0.008*

The relationship between the level of visual acuity and Self Injurious Behaviours in children with Septo Optic Dysplasia and Optic Nerve Hypoplasia.

Using the Social Communication Questionnaire, children who had complete visual loss tended to report Self Injurious Behaviours more frequently than children who had impaired vision and these differences were significantly statistically different. Table 6.7.2 summarises these findings.

Table 6.7.2: Mean, Standard Deviation (SD) and statistical analysis between the degree of visual impairments in children with Septo Optic Dysplasia and Optic Nerve Hypoplasia and the Presence/ or Absence of Self Injurious Behaviours.

Presence (+) or Absence (-) of SIB	Level of Vision	N (-)/ (+)	% (-)/(+) of SIB	X^2	*df*	*p-value*
- SIB	Impaired	20	70.0			
	Blind	6	30.0			
+ SIB	Impaired	8	57.1	3.87	1	.05*
	Blind	6	42.9			

**Statistical significance at .05*

The impact of Sensory Processing Disorders on Self Injurious Behaviours in children with Septo Optic Dysplasia and Optic Nerve Hypoplasia.

There were statistically significant differences between the presence and absence of Self Injurious Behaviours (as identified by the SCQ) and the Total Sensory score, the sub-domain, Under-responsive/ Seeks sensation and Tactile Sensitivity of the Short Sensory Profile. Table 6.7.3 summarises these findings.

Table 6.7.3: Mean, Standard Deviation (SD), and statistical analysis between the Short Sensory Profiles Total and sub-domain levels according to the Presence/absence of Self Injurious Behaviours in children with SOD/ONH

Short Sensory Profile	Presence (+) or Absence (-) SIB	N	Mean	SD	*U*	*df*	*p-value*
Total Sensory Score	- SIB	27	128.73	23.11	95.00	2	.01*
	+ SIB	14	108.07	20.08			
Auditory Sensitivity	- SIB	27	6.58	2.37	112.50	2	.02***
	+ SIB	14	4.73	2.43			
Movement Sensitivity	- SIB	27	13.35	3.03	153.00	2	.27
	+ SIB	14	12.13	3.44			
Under Responsive /Seeks Sensation	- SIB	27	23.50	7.93	101.50	2	.01*
	+ SIB	14	16.93	7.08			
Auditory Filtering	- SIB	27	19.38	6.79	157.00	2	.20
	+ SIB	14	17.40	4.45			
Low Energy	- SIB	27	21.46	6.86	121.50	2	.05**
	+ SIB	14	16.40	7.99			
Tactile Sensitivity	- SIB	27	30.15	5.35	59.50	2	.00**
	+ SIB	14	22.27	5.36			
Taste and Smell Sensitivity	- SIB	27	14.65	5.13	139.00	2	.13
	+ SIB	14	11.80	5.99			

**** Statistically significant at 0.05;**Bonfferonni correction at 0.0063 for statistical significance, * statistical significance at 0.01.*

The relationship between Autistic Spectrum Disorders in children with Septo Optic Dysplasia and Optic Nerve Hypoplasia and Self Injurious Behaviours

Children who scored above the cut-off point for Autistic Spectrum Disorders on the Social Communication Questionnaire, Gilliam Autism Rating Scale, the Autism Diagnostic Observation Schedule or who had received a diagnosis of autism from a Clinician were more likely to show Self Injurious Behaviours than children who did not

meet the cut-off point for, or had received a diagnosis of, Autistic disorder. Table 6.7.4 summarises these findings.

Table 6.7.4: The Presence/absence of SIB according to scoring above the cut-off point for ASD on the Social Communication Questionnaire, the Gilliam Autism Rating Scale, the Autism Diagnostic Observation Schedule and Clinician Diagnosis.

Raw SCQ Score	Presence (+) or Absence (-) of SIB	N	Mean	SD	*U*	*df*	*p-value*
Communication Domain	- SIB	28	5.04	3.20	67.00	2	.000**
	+ SIB	14	6.79	4.67			
Social Interaction Domain	- SIB	28	4.11	4.10	86.00	2	.004*
	+ SIB	14	8.43	3.85			
Stereotyped Behaviours Domain	- SIB	28	2.67	2.73	82.00	2	.002*
	+ SIB	14	5.36	2.20			

** Statistically significant at 0.05;*** statistical significance at 0.01.*

The raw scores of the Social Communication Questionnaire's sub-domain levels shown in table 6.7.5, reported that children with Self Injurious Behaviours had statistically significant higher means on the Communication, Social Interaction and Repetitive/ Stereotyped behaviours domain scores (i.e. more impaired) compared to children without Self Injurious Behaviours.

Table 6.7.5: Differences between the presence and absence of Self Injurious Behaviours on the Social Communication Questionnaires sub-domain levels in children with Septo Optic Dysplasia and Optic Nerve Hypoplasia.

ASD tools	Presence (+) or Absence (-) of SIB	Above/below the Cut-off for ASD				X^2	*df*	*p-value*
SCQ	- SIB	Below	17	Above	8	14.25	1	.00 **
	+ SIB	Below	1	Above	14			
GARS	- SIB	Below	21	Above	4	10.58	1	.00**
	+ SIB	Below	5	Above	10			
ADOS	- SIB	Below	19	Above	7	8.32	1	01**
	+ SIB	Below	4	Above	11			
Clinician	- SIB	Below	21	Above	5	5.11	1	.03*
	+ SIB	Below	7	Above	8			

***Bonfferonni correction at 0.0125;** statistical significance at 0.01*

The Types of Self Injurious Behaviours using the CBQ

The following sections will only deal with children who displayed Self Injurious Behaviours according to the SCQ. The prevalence of Self Injurious Behaviours (SIB) in the sample was 33% (n=13) for children diagnosed with Septo-Optic Dysplasia/Optic Nerve Hypoplasia, as one family did not return the CBQ and MAS. The CBQ reported Physical Aggression (e.g. punching, pushing, kicking, pulling and grabbing) in 85% of the children, 77% demonstrated disruption and destruction of property or the environment, and 85% exhibited stereotyped behaviours (e.g. rocking, twiddling, and eye pressing and constant hand movements).

The percentage of children showing a specific SIB in a repetitive manner (>twice in succession) included 62% of the group, hitting themselves with a body part (slaps head or face) included 38% of children, hitting self against surface or object 31%, hitting self with object was 46%, biting themselves 23% pulling (pulling hair or skin), 46% displayed rubbing or scratching self, and 31% of children inserted their fingers or objects (e.g. eye poking). Table 6.7.6 shows individual participant characteristics and types of SIB displayed (n =13).

Table 6.7.6: Child characteristics and presence (+) or absence (-) of particular types of Self Injurious behaviours

D	Vision	G	SCQ	Bites self	Pulls Hair Skin	Scratch Rubs/ self	Inserts finger/ Objects	Hits self with body	Hits self against surface	Hits self with object
ONH	Poor	F	26	-	+	+	-	+	+	+
ONH	Blind	M	30	+	+	-	-	+	-	-
ONH	Poor	F	25	-	-	+	-	+	+	-
SOD	Blind	F	23	-	+	+	+	+	-	-
SOD	Blind	F	34	-	-	+	-	-	-	+
SOD	Blind	F	27	+	-	-	-	+	-	+
SOD	Blind	M	22	-	-	+	+	+	+	-
SOD	Blind	M	22	-	-	-	-	+	+	-
SOD	Poor	F	22.	+	-	-	+	-	-	-
SOD	Poor	F	26	-	-	-	-	-	-	-
SOD	Poor	M	22	+	-	+	-	+	+	+
SOD	Poor	M	15	+	-	-	+	-	-	-
SOD	Blind	M	23	+	-	-	-	-	-	-
				6	3	6	4	8	5	4

**+ shows behaviour, - behaviour is absent*

The Motivations for Self Injurious Behaviours according to the Motivation Assessment Scale

Overall, the mean score for each domain of the MAS was, Sensory Motivations 2.67(SD=1.43), Escape 3.03 (SD=1.26), Attention 2.10 (SD=1.57) and Tangible 3.36 (SD=1.87).

The relationship between children's level of visual acuity and their Motivations for Self-Injurious Behaviours according to the Motivation Scale (MAS)

No statistically significant differences were reported between children and their level of visual acuity. Table 6.7.7 shows little difference between the means of children with poor vision and children with complete visual loss.

Table 6.7.7: The relationship between children's level of visual acuity and their Motivations for Self Injurious Behaviours according to the Motivation Scale (MAS)

MAS	Vision	N	Mean	SD	X^2	*df*	*p-value*
Sensory	Poor	6	10.33	8.21	13.00	9	.16
	Blind	7	9.71	3.40			
Escape	Poor	6	10.50	5.01	10.	9	.33
	Blind	7	13.57	6.21			
Attention	Poor	6	8.17	7.55	7.64	7	.37
	blind	7	8.29	5.21			
Tangible	Poor	6	14.17	7.65	6.96	9	.64
	Blind	7	12.14	7.65			

The relationship between intellectual disability and children's Motivations for Self Injurious Behaviours according to the Motivation Assessment Scale (MAS)

Weak correlations were reported between the four Motivation Assessment Scales and the Adaptive Behaviour composite, the sub-domain of Expressive language and domain of socialisation of the Vineland Adaptive Behaviour Scale. Table 6.7.8 summarises these findings.

Table 6.7.8: Pearson correlations between the four Motivation Assessment Scales and the Adaptive Behaviour composite, the sub-domain of Expressive language and domain of socialisation of the Vineland Adaptive Behaviour Scale.

VABS	The Motivation Assessment Scale			
	Sensory	Escape	Attention	Tangible
Expressive Language	-.317	-.390	-.487*	-.499*
Social Domain	-.331	-.190	-.230	-.199
ABC	.001	-.047	.054	-.147

Difference between Autism and children's Motivations for Self Injurious Behaviours according to the Motivation Assessment Scale (MAS)

There were no statistically significant differences between the diagnosis of autism from a Clinician and the Motivations for Self Injurious Behaviours, table 6.7.9 summarises these findings.

Table 6.7.9: The differences between children's Motivations for Self Injurious Behaviours according to the Motivation Scale (MAS) and receiving a diagnosis of autism from a clinician.

MAS	Clinician Diagnosis	N	Mean	SD	X^2	*df*	*p-value*
Sensory	-	5	10.00	7.78	20.00	2	1.0
	+	8	10.00	4.87			
Escape	-	5	12.20	4.38	12.00	2	.28
	+	8	12.13	6.66			
Attention	-	5	9.80	7.16	14.00	2	.44
	+	8	7.25	5.65			
Tangible	-	5	13.80	8.38	18.00	2	.83
	+	8	12.63	7.29			

6. 6. Discussion

The current study is the first to have assessed the presence of maladaptive behaviours and sensory processing disorders in children with Optic Nerve Hypoplasia and Septo Optic Dysplasia.

Using the Social Communication Questionnaire, Gilliam Autism Rating Scale and the Autism Diagnostic Observation Schedule, children with Septo-Optic-Dysplasia, Optic Nerve Hypoplasia and isolated Hypopituitarism reported differences in the prevalence of Restrictive Repetitive and Stereotyped behaviours. Secondly, the Short Sensory Profile also found differences between the reporting of Sensory Processing Disorders in children with Septo-Optic-Dysplasia, Optic Nerve Hypoplasia and isolated Hypopituitarism. Using the Challenging Behaviour Questionnaire and the Motivation Assessment Scale, a small number of children reported Self Injurious Behaviours and they demonstrated varying typographies and motivation towards these behaviours.

Overall findings

The present study reported that autistic phenomenology, varying degrees of intellectual disability and/or visual loss increased children's vulnerability to maladaptive behaviours and sensory processing disorders. Some children with autistic disorders and Optic Nerve Hypoplasia/Septo Optic Dysplasia presented with the classic triad of impairments (Wing, 1969) and the associated features of autistic disorders. However, children without autism also presented with maladaptive behaviours and sensory processing disorders. These findings indicate that such phenomenologies may be associated with greater degrees of neurological impairments and sensory deprivation rather than Autistic Spectrum Disorders.

The reporting of Restrictive, Repetitive and Stereotyped Behaviours in children with Septo-Optic Dysplasia and Optic Nerve Hypoplasia.

Overall, children with Optic Nerve Hypoplasia and Septo-Optic Dysplasia showed more occurrences of Restrictive, Repetitive and Stereotyped behaviours in comparison to children with isolated Hypopituitarism. The prevalence of Restrictive, Repetitive and Stereotyped behaviours in the present study was 42% to 57%, compared to only 25% to 45% in the retrospective study carried out by Shaffer *et al.,* (2008). The results of the study are also consistent with research which showed that Repetitive behaviours were more prevalent in children with intellectual disability (Dykens, 2000), and visual impairments (Keller, 1958). Overall, Repetitive behaviours were strongly related to impairments in Communication and Social Interaction, which confirms that these three characteristics occur commonly together (Wing & Gould, 1979). Furthermore, no differences were reported between the level of visual loss and Restrictive, Repetitive and Stereotyped

behaviours, and this occurrence persisted even when intellectual disability was used as a covariate. Thus, indicating that intellectual disability, explained the differences between Restrictive, Repetitive and Stereotyped behaviours rather than visual loss.

Looking at the Adaptive Behaviours of children using the Vineland Adaptive Behaviour Schedule, no relationship was reported between Restrictive, Repetitive and Stereotyped behaviours and the, sub-domains of Receptive Language, Expressive language, and the domains of Socialisation and Daily Living Skills. This finding contradicts the reports of Bak, (1999) who reported high correlations between the severity of Stereotypyies and intellectual disability, Receptive and Expressive Language Skills. However, the overall Adaptive Behaviour Composite was moderately negatively correlated with the Stereotypies Domain of the Autism Diagnostic Observation Schedule and the Social Communication Questionnaire, indicating that, Restrictive, Repetitive and Stereotyped behaviours did occur more in children with greater degrees of intellectual disabilities. In addition, children who showed impairments in sensory processing demonstrated a greater presence of Restrictive, Repetitive and Stereotyped Behaviours.

Differences in prevalence rates of Restrictive Repetitive and Stereotyped Behaviours reported by Shaffer *et al.,* (2008) and the present study can be attributed to the data collection methodology. The present study used parental reports and direct observations, and Shaffer *et al.,* (2008) used retrospective clinical data which was collected over thirty years. This increase can also be attributed in the present study to parent's greater recognition of these behaviours, and the broader classification of Autistic Spectrum Disorders, which has emerged over the last thirty years. Hence, the increase in Restrictive Repetitive and Stereotyped behaviours in the present study may reflect the overall increase in reporting of Autistic Spectrum Disorders. Even so, as children with Optic Nerve

Hypoplasia and Septo Optic Dysplasia can display both intellectual disability and differing levels of visual impairment, it cannot be deduced which factor contributed exclusively to Restrictive Repetitive and Stereotyped behaviours in these children.

Theoretical explanations for the present occurrence of Repetitive behaviours in children with Septo-Optic Dysplasia and Optic Nerve Hypoplasia are supported by Baumeister's, (1978) theory, that Restrictive Repetitive and Stereotyped behaviours provide sensory stimulation and specifically, stimulation of the vestibular system (Russel, 1994). Furthermore, Restrictive Repetitive and Stereotyped behaviours may be part of the behavioural phenotype of children with visual loss, and not autistic in their origin, and they may also have an adaptive function (Gense & Gense, 1994).

In summary, Restrictive Repetitive and Stereotyped behaviours in children with Septo-Optic Dysplasia and Optic Nerve Hypoplasia are strongly associated with greater degrees of intellectual disability, and sensory processing difficulties, rather than those children's level of visual acuity. Furthermore, Restrictive Repetitive and Stereotyped behaviours are also closely related to impairments in Communication and Social interaction which demonstrated the common co-occurrence of the triad of impairments in the present cohort of children.

The identification of Sensory processing Disorders in children with Septo-Optic Dysplasia and Optic Nerve Hypoplasia.

The present study demonstrated that the degree of visual loss was the best predictor of sensory processing disorders in children with Septo Optic Dysplasia and Optic Nerve Hypoplasia. Hormonal loss and the level of intellectual disability did not contribute to the differential reporting of sensory processing disorders on the Short Sensory Profile.

However, children who scored above the cut-off point for Autistic Spectrum Disorders on the Social Communication Questionnaire's Total and sub-domain levels tended to have more "Definite Differences" in their processing of sensory information.

Children with severe and profound visual loss showed the greatest impairments on the Short Sensory Profiles sub-domains of Auditory Sensitivity, Under-responsiveness/Seeking Sensation and Weak Energy. Overall children with severe to profound visual loss showed "Definite Differences" in their overall processing of sensory information.

The results also suggest that autistic phenomenology and sensory processing disorders commonly co-occur together, but greater severities of visual loss are also attributable to sensory processing disorders. However, the origin of blind children's sensory impairments may be different to that of sighted autistic children. For instance, the impairments seen in the sub-domains of Under-responsiveness/Seeking Sensation and Weak Energy of the Short Sensory Profile, by blind children can be explained by the environmental constraints placed upon children with visual loss, as visual loss inevitably leads to reduced incidences of exploratory behaviours of the children's immediate environment (Troster & Brambring, 1994).

The constraints the blindness poses on the types of activities that a blind individual can engage in, explains the lack of responsiveness that children exhibited in their processing of sensory information (Lewis, Norgate, Colllis & Reynolds, 2000). Furthermore, Lowenfeld (1973) postulated that some of the autistic-like phenomenology in the blind could be explained by the reduced ranges, and variety of experiences that blind children encounter. This in turn affects blind children's ability to move around, and manipulate their environment, which inevitably makes a blind child appear less responsive

to their sensory environment, due to their reduced physical exploration. To further support the Lowenfeld theoretical hypothesis, Chase, in 1972, reported similarities between autistic children, children who had endured early sensory or maternal deprivation, and children with impaired vision

Therefore, the question which arises is, how does one differentiate between sensory impairments due to idiopathic autism, and/or a result of organic brain abnormalities, from that of sensory impairments, due to visual deprivation (Tager-Flusberg, 2005). Drawing from the parallels from studies examining quasi-autistic features in Romanian children by Rutter *et al.*, (1999), sensory impairments were also reported which remained even after children were adopted into U.K families. In summary, Figure nine shows the possible alternative pathways to sensory impairments for children with autism, intellectual disability and visual loss in the present study.

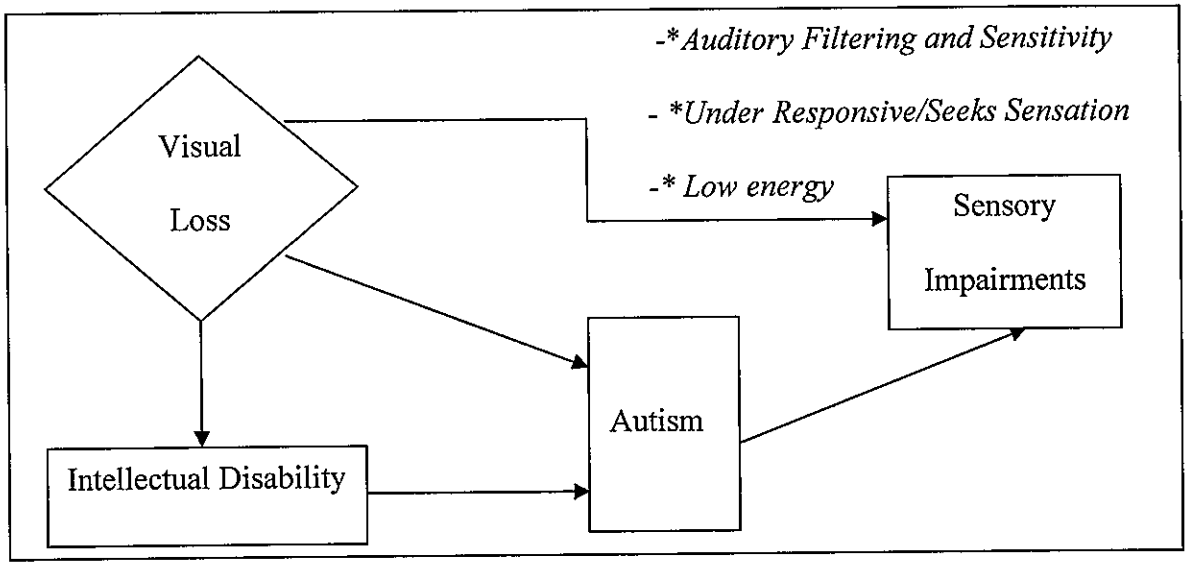


Figure nine: The alternative pathways to sensory impairments for children with autism, intellectual disability and visual loss.

The identification of Self Injurious Behaviours in children with Septo-Optic Dysplasia and Optic Nerve Hypoplasia.

Statistically significant differences were reported between the Adaptive Behaviour Composite of the Vineland Adaptive Behaviour Scale, severity of visual loss and the presence or absence of Self Injurious Behaviours. Furthermore, the Short Sensory Profile reported that all domains, apart from the Movement Sensitivity, Taste and Smell, and Auditory Filtering Domain, reached various degrees of statistically significant difference. Looking at the association between autistic behaviours and Self Injurious Behaviours, significant statistical associations were reported, with a higher proportion of children with Self Injurious Behaviours scoring above the cut-off point for Autistic Spectrum Disorders on the Social Communication Questionairre, Autism Diagnostic Observation Schedule, and Gilliam Autism Rating Scale. The sub-domains of the Social Communication Questionnaire also showed statistically significant differences between the presence and absence of Self Injurious Behaviours. These results suggest, that the risk markers for Self Injurious Behaviours are the degree of intellectual disability, sensory processing impairments, severity of autistic behaviours, and children's level of visual function.

Looking only at the characteristics of children, who displayed Self Injurious Behaviours, all children scored above the cut- off point for Autistic Spectrum Disorders on the Social Communication Questionnaire, and had greater degree of intellectual disability. Most commonly, children hit themselves with their hands. The motivations for Self Injurious Behaviours most commonly included Sensory Stimulation, Escape and Tangible reasons. Interestingly, "Escape" showed a high mean motivation score, which is usually an indicator of a task being too difficult, or uninteresting to the child. It would be expected that children with visual loss would not display "Escape" behaviours so often, due to not

having a visual target to orientate towards, however the study demonstrated the SIB are used to "Escape" from their immediate environment. High scores on the "Tangible" category usually result when reasonable requests (e.g., wanting snacks or a change in activities) are being ignored.

Previous research has indicated that Self Injurious Behaviours provided children with Sensory stimulation (Edelson, 1984; Maisto *et al.*, 1978), and this was reported on the Motivation Assessment Scale and confirmed by the Short Sensory Profile. However, Sensory Stimulation appeared to be a secondary reason for a motivation towards Self Injurious Behaviours. Children with Septo Optic Dysplasia and Optic Nerve Hypoplasia tended to use Self Injurious Behaviours as a means of communication.

Limitations to present study

For the assessment of Restrictive Repetitive and Stereotyped Behaviours and sensory processing disorders there was a reliance on parental reporting through rating scales, and this could have resulted in an over representation of these behaviours. Direct observation of these behaviours was only achieved during the Autism Diagnostic Observation Schedule, which usually take 30-40 minutes to complete and the duration of this assessment may have been too short in order to identify Restrictive Repetitive and Stereotyped Behaviours in children. Furthermore, it is not known how age impacted on these behaviours and research has demonstrated that Restrictive Repetitive Behaviours occur more commonly in younger children.

As this is the first study to asses Self Injurious Behaviour in children with Septo Optic Dysplasia and Optic Nerve Hypoplasia, it is not known whether these children differ from children with other neurodevelopmental disorders who also show Self

Injurious Behaviours. In addition, the syndromes themselves may not predispose children to Self Injurious Behaviours, but the severity of associated visual loss and intellectual disability found in the syndromes may do so.

Suggestions for follow up research

There are a number of validated assessment tools available to measure Restrictive Repetitive and Stereotyped Behaviours. Future research would need to use these tools but with modifications which would take into consideration children's severe to profound levels of visual loss. Furthermore, direct observations in a number of environmental settings would provide an insight into the triggers for maladaptive behaviours. Future research needs to address whether children with different neurological impairments, display different types of sensory impairments. Furthermore, the study has demonstrated that the intact senses of children with Septo Optic Dysplasia and Optic Nerve Hypoplasia can be greatly affected, and this ultimately influences their expressed behaviours.

Furthermore, the motivations for Self Injurious Behaviours appear to multi-factorial, and include sensory stimulation, attention, escape and tangible reasons. For these reasons it is important to assess the motivations for Self Injurious Behaviours for each individual child. This would include a functional assessment of the when, where, how often a behaviour occurs and at what intensity a particular Self Injurious Behaviour manifests itself. From the functional assessment of a child's Self Injurious Behaviours, preventative strategies and interventions can be incorporated to reduce Self Injurious Behaviours.

Implications and Summary of the present study

Early educational programmes need to include methods to help children to integrate, and use effectively their intact senses in order to reduce some of their hyposensitivity and hypersensitivities to sensory information. What is not known is whether the origin of blind children's autistic-like behaviours are an antecedent of their sensory dysfunctions, or rather due to deep neurological impairments. However, co-morbid neurological damage which leads to varying levels of intellectual disability in the blind creates the problem of deducing how visual loss affects other intact senses. The relationship between sensory processing problems may include maladaptive behaviours, which may be the child's way of getting some sensory input. The present study demonstrates the close relationship between maladaptive behaviours and sensory processing disorders.

CHAPTER SEVEN

GENERAL DISCUSSION

7.1 Aims of the Chapter

Chapter Seven will firstly evaluate the empirical chapters of the thesis in respect to the original research objective. Particular emphasis will then be afforded to previous research, the present findings and the theoretical consequences of the thesis. This will aid in creating a final model of autistic phenomenology in children with Septo Optic Dysplasia and Optic Nerve Hypoplasia. The limitations of the present study and any suggestions for future research will also be outlined. Furthermore, the clinical importance and implications of these findings will be discussed. Lastly, a final summary of the conclusions will be discussed.

7.2 Overall findings of the thesis

The overall findings of the thesis suggest that Autistic Spectrum Disorders are prevalent in children with Septo Optic Dysplasia and Optic Nerve Hypoplasia, but not in children with isolated Hypopituitarism. Susceptibility to autistic disorders, in children with Septo Optic Dysplasia and Optic Nerve Hypoplasia is closely related to children's degree of intellectual disability, and also their visual loss, but not their hormone deficiencies. More specifically, the thesis reported that greater severities of neurological impairments left children more vulnerable to autistic disorders. For these reasons, Autistic Spectrum Disorders should be considered as an associated disorder in children with the syndromes of Septo Optic Dysplasia and Optic Nerve Hypoplasia. Furthermore, sensory processing disorders and Self Injurious Behaviours, which are already commonly reported in children with autistic disorders, intellectual disability or visual loss, were also reported in children with Septo Optic Dysplasia and Optic Nerve Hypoplasia, but again

these symptomatologies were reported in greater numbers for children with greater levels of intellectual disability and visual loss. Overall, children with Septo Optic Dysplasia and Septo Optic Dysplasia showed the classic triad of impairments (Wing & Gould, 1979) and the associated symptomatology of sensory processing disorders and Self Injurious Behaviours.

7.3 Evaluation of the results and findings of the empirical chapters of the thesis

The literature review in the Chapter Four reported that visual impairments in children with Optic Nerve Hypoplasia and Septo Optic Dysplasia can lead to certain developmental sequelae, such as Autistic Spectrum Disorders. This occurrence has been previously documented by a handful of researchers such as, Bahar, Brody, McCann, Mendiola and Slott (2003), Ek, Fernell and Jacobson (2005), Garcia-Filion *et al.*, (2008), Haddad and Eugster (2005), and most recently by Parr, Shaffer, Salt, and Dale (2008). Research into Optic Nerve Hypoplasia and Septo Optic Dysplasia has largely focused upon epidemiological and genetic studies, and there has been a lack of focus on assessing the behavioural and cognitive aspects of children with these syndromes. An explanation for the sparse literature available in this area is that research can encounter methodological problems, with the added complexity of within group variability, and this has challenged previous researchers (Pring, 2005).

Without a systematic methodical framework to work within, or to work towards, Chapter Three firstly considered the methodological issues of assessing autistic phenomenology in children with Septo Optic Dysplasia and Optic Nerve Hypoplasia by reviewing literature on the developmental pathway of children with visual loss. The literature review recognised that children with visual loss elicited their social and

communicative behaviours through their intact senses in a very unique way. Therefore, future assessment tools needed to be sensitive to this.

Chapter Three also examined a range of diagnostic tools which have been used previously by researchers and Clinicians for the assessment of Autistic Spectrum Disorders. The aim of this review was to assess whether adaptations or exclusions to the materials, and scoring criterion of a chosen assessment could be made, in order to give children with visual loss the maximum opportunity to demonstrate their social and communicative behaviours.

The Autism Diagnostic Observation Schedule was selected due to its previous use with children with various clinical syndromes and intellectual disabilities (Bonati *et al.*, 2007; Klien-Tasem, Mervis, Lord & Phillipos, 2007; Milner *et al.*, 2005). The Autism Diagnostic Observation Schedule is considered the "gold standard" of diagnostic tools to use for the assessment of autistic disorders, due to its strong psychometric properties and its method of administration.

The empirical component of Chapter Three, reported that typically developing children, children with autistic disorders and children with intellectual disability performed similarly on the original and modified Autism Diagnostic Observation Schedule. This demonstrated that, regardless of symptomatology, the modified and original Autism Diagnostic Observation Schedule elicited similar responses. Secondly, when visually impaired children with severe intellectual disability were compared on the original and modified modules of the Autism Diagnostic Observation Schedule similar responses were elicited on both versions.

The present study was the first to systematically assess for autistic disorders within this complex clinical cohort, and the observational nature of this assessment gave the opportunity to directly observe the social and communicative strategies adopted by

children with visual loss. Children's responses to auditory stimuli included an initial stilling, which indicated that the child had acknowledged the sound and this was usually followed by a turning towards the source of the sound during tasks in module one of the assessments. These behaviours indicated to the researcher that the child was ready to engage and participate in the activity. Furthermore, the bubble gun task showed that children responded well to the sensation of the bubble touching their skin and the accompanying stream of air. These direct observations during the modified Autism Diagnostic Observation Schedule showed that children with visual loss were able to communicate their wants and needs through the coordination of motor activities in response to the appropriate sensory stimuli. These behaviours were only recorded due to the direct observations by the researcher, and this would not have been reported if rating scales had been used. Furthermore, the study further endorsed the use of appropriate toys within the modified Autism Diagnostic Observation Schedule which helped to provide appropriate stimulation to children through their intact senses.

Even though Chapter Three reported that the modified Autism Diagnostic Observation Schedule could be used on children with moderate learning disabilities and visual impairments, when it is used on children with severe to profound levels impairments, the scores should be interpreted with caution. This recommendation is based on previous research by Gray, Bruce, Tonge and Sweeney (2007) who state that caution is needed when interpreting autistic behaviours in children with low developmental ages, and the elevated algorithm scores reported on the modified Autism Diagnostic Observation Schedule. Most importantly, the Chapter demonstrated that without an assessment tool that can be used on all children with complex symptomatologies, such children can often be overlooked for the diagnosis of autistic

disorders, and this can leave children vulnerable to further developmental delays, due to a lack of early interventions and appropriate educational provisions.

Due to the lack of research into the measurement of autistic disorders in the blind, consequently there is consequently an absence of a validated psychometric tool to use for the visually impaired (Dale, 2005). To address this issue, Chapter Four aimed to measure the differential reporting of autistic disorders between four commonly used assessment tools. The results reported that Clinician diagnosis, the Autism Diagnostic Observation Schedule, and the Social Communication Questionnaire gave good levels of validity, but not the Gilliam Autism Rating Scale. This confirmed the importance of using appropriate diagnostic assessments for the measurement of autistic disorders, as differential diagnoses were reported depending on which type of assessments was used.

Differential diagnoses could be explained by the use of parental, researcher observations, and Clinician diagnosis. The experience of the Clinician and the incorporation of other developmental information by the Clinician were likely to provide the most accurate diagnosis of autism. Even so, the Social Communication Questionnaire can be used as a screening tool for autistic disorders, and the adapted Autism Diagnostic Observation Schedule can provide Clinicians with an objective measurement of autistic behaviours in children with visual loss. Furthermore, the degree of visual loss and intellectual disability in children should be considered when interpreting the psychometric properties of instruments used to assess autism within a blind population. Specifically, Lord and Risi (1998) state that diagnostic tools lose their specificity, when used with children with profound learning disabilities or high functioning adults, and this would also be expected with the modified Autism Diagnostic Observation Schedule.

Considering the two syndromes, Optic Nerve Hypoplasia and Septo Optic Dysplasia, studies using small cohorts of patients or retrospective patient records have been published to date. The research studies by Parr *et al.,* (2008), Ek *et al.*, (2005), Pring & Ockelford (2005), Bahar *et al.*, (2003), confirm a common co-occurrence of autism and Septo Optic Dysplasia and Optic Nerve Hypoplasia. Chapter Four, reported that of the fifty-six children who were evaluated on all three measures for Autistic Spectrum Disorders, twenty-four children met the criteria for further investigation of pervasive developmental disorders using the Social Communicative Questionnaire, eighteen met the criteria for autism using the Autism Diagnostic Observation Schedule, and fourteen met the criteria for Autism Spectrum Disorders according to the Gilliam Autism Rating Scale. Furthermore, Clinician diagnosis was received by fourteen children, which reiterates the disparity of reporting of Autism Spectrum Disorders amongst children.

The study by Parr *et al.*, (2008) reported that the percentage of Autistic Spectrum Disorders in children with Septo Optic Dysplasia and Optic Nerve Hypoplasia as 22%, in comparison to the present study, the Social Communication Questionnaire reported 44%, the Autistic Diagnostic Observation Schedule 32%, the Gilliam Autistic Rating Scale 25%, and Clinician Diagnosis was 20%. These differences can be attributed to the differences in the methodology used, specifically the utilisation of parental, researcher or Clinician assessment of autism and the general rise in the reporting of autistic disorders. Notably, similar percentages of autism were reported by Parr *et al.*, (2008), and Clinician diagnosis in the present study.

In support of the present findings of Chapter Four, previous research has reported that both the Social Communication Questionnaire and Autism Diagnostic Observation Schedule have shown good agreement levels (Howlin & Karpf, 2004). Chapter Four and

previous research, both emphasise that diagnostic assessments should not be used in isolation, but in conjunction with Clinician diagnosis, and with the incorporation of children's full developmental histories. This practice will ensure that Clinicians are provided with a complete clinical picture of each child.

Statistically significant differences were found between measures of intellectual disability, and the Total, Social Interaction and Communication domain of the Autism Diagnostic Observation Schedule. The regression analyses reported that intellectual disability, better accounted for the severity of autistic phenomenology in children with Septo Optic Dysplasia and Septo Optic Dysplasia, but this may have also accounted for the reported differential reporting between the scales. Both the findings of Mukaddes *et al.*, (2007) and the results of the present study suggest that children with blindness and autism have greater neurological impairment, and greater degrees of visual impairment.

Chapter Five considered the cognitive and adaptive behaviours of children within the present clinical cohort. The Chapter demonstrated the importance of not relying on a single measure of intellectual disability, as derived from the Adaptive Behaviour Composite of the Vineland Adaptive Behaviour Scale, but also using the domains and sub-domains of the Vineland Adaptive Behaviour Scale, when assessing children's developmental profiles. This practice helped to identify specific impairments in children that face within their adaptive behaviours.

Children with Septo Optic Dysplasia showed greater impairments in the sub-domain of Receptive Language of the Vineland Adaptive Behaviour Scale, which assesses how children learn to listen, and understand language. These children also showed the most impairments in the sub domain of Interpersonal Skills of the Vineland Adaptive Behaviour Scale, which assesses imitation, and the showing of emotions, in comparison to children with Optic Nerve Hypoplasia and isolated Hypopituitarism. The

findings of this investigation endorse the use of fine grained approach to the analyses of adaptive behaviours.

There was also a strong relationship between the domains of the Vineland Adaptive Behaviour Scale and the Slossen Intelligence Scale Revised, but not on the Adaptive Behaviour Composite of the Vineland Adaptive Behaviour Scale. This suggests that both cognitive and adaptive behaviours are interrelated and need to be assessed when looking at autistic phenomenology. Chapter Five, reported that particular aspects of adaptive behaviour, such as Expressive Language Skills, Personal Skills, Community, Daily Living Skills and Interpersonal Skills were statistically different between non autistic, and autistic children. Furthermore, differences were also reported between the Slossen Intelligence Test and autistic and non autistic children.

Study Five, confirmed the need for more research to help to delineate between the cognitive and adaptive functioning differences in children with visual impairments and/or intellectual disability. It is estimated that at least 25% to 63% of individuals with a visual impairment, also have some form of intellectual disability (Janicki, & Dalton; 1998, Lavis, 1994). Severe levels of visual impairment are usually directly proportional to greater levels of intellectual disability (Warburg, 2001), but how this impacts on cognitive and adaptive behaviours in children with visual impairments and intellectual disability has received little attention. Knowing that both visual loss and intellectual disability are contributing factors to autistic phenomenology (Rogers, 1995), and characteristic of the syndromes of Septo Optic Dysplasia and Optic Nerve Hypoplasia, a specific measure for the assessment of the cognitive and adaptive behaviours of the blind needs to be created.

The final empirical Chapter measured the occurrence of maladaptive behaviours and sensory processing disorders Chapter Six firstly reported that the degree of visual

loss was the best predictor of sensory processing disorders in children with Septo-Optic Dysplasia and Optic Nerve Hypoplasia. Hormonal loss and the level of intellectual disability did not contribute to the differential reporting of sensory impairments on the Short Sensory Profile. However, children who scored above the cut-off point for Autistic Spectrum Disorders on the Social Communication Questionnaire's Total and sub-domain levels tended to have more "Definite Differences" in their processing of sensory information.

Children with severe and profound visual loss showed the greatest impairments on the Short Sensory Profiles sub-domains of Auditory Sensitivity, Under-responsiveness/Seeking Sensation and Weak Energy. Overall, children with severe to profound visual loss showed "Definite Differences" in their overall processing of sensory information. These results suggest that autistic phenomenology, and sensory processing disorders commonly co-occur together, but greater severities of visual loss also result in sensory processing disorders.

However, co-morbid neurological damage which leads to varying levels of intellectual disability in the blind creates the problem of deducing how visual loss affects other intact senses. Previous sensory deprivation studies (Doman, 1984) have shown that sudden and nearly complete deprivation of stimulation through the five senses can lead to autistic-like behaviours (e.g. withdrawal, stereotyped movements), but these problems are reversible with proper stimulation or removal from the deprived environment. The study by Rutter *et al.*, (1999), however found that sensory impairments tended to persist in children even after their removal from their deprived environment. Gibbons, (2005), suggests that if the origin of autistic behaviours is viewed as a result of abnormal perception, this may explain some of the frequently observed autistic-like behaviours in the blind. Similarly, Andrew and Wyver's (2005) question whether blind children follow

a different pathway to autistic behaviours to that of sighted autistic children, and this pathway could be due to sensory processing disorders.

Secondly, Chapter Six considered the high incidences of repetitive behaviours in children with severe and profound visual loss, which has been previously reported by a number of researchers (Bak, 1999; Dehra, 1981; Hallenbeck 1954a; Fazzi *et al.*, 1999; Keller 1958; McHugh & Lieberman, 2003; Parr, *et al.*,, 2008, Troster *et al.*, 1991; Tröster, Brambring, & Beelmann, 1991). The chapter reported that greater degrees of intellectual disability, and sensory processing difficulties, explained the occurrence of Restrictive, Repetitive and Stereotyped behaviours in the present cohort, rather than children's level of visual acuity.

Children with Optic Nerve Hypoplasia and Septo-Optic Dysplasia showed more occurrences of repetitive behaviours in comparison to children with isolated Hypopituitarism. A prevalence of Repetitive behaviours in the present study was 42% to 57%, compared to only 25% to 45% in the retrospective study carried out by Shaffer *et al.,* (2008). Differences in prevalence rates of repetitive behaviours can be attributed to the data collection methodology, as the present study used parental reports and direct observations, compared to retrospective clinical data, collected over thirty years by Dale *et al.*, (2008). This increase can also be attributed to the greater recognition by parents of Repetitive Behaviours and the broader classification of Autistic Spectrum Disorders emerging over the last thirty years. Hence, the increase in repetitive behaviours in the present study could be linked to the overall increase in reporting of Autistic Spectrum Disorders. Overall, repetitive behaviours were also strongly related to impairments in communication and social interaction, which confirms that these three characteristics occur commonly together (Wing & Gould, 1979).

It has been argued that stereotypes may have a functional value for children who are blind, compared to sighted autistic children (Troester, Brambring, & Beelmann, 1994). For sighted autistic children, restrictive, repetitive behaviours provide sensory stimulation, by increasing arousal levels when stimulation from the environment is low (Baumeister, 1978; Forehand & Baumeister, 1971). However, children with visual loss may use repetitive behaviours to make sense of their world by aiding exploration of their immediate environment (Gense & Gense, 2004).

Lastly, Chapter Six was the first study to assess Self Injurious Behaviour in children with Septo Optic Dysplasia and Optic Nerve Hypoplasia. The prevalence of Self Injurious Behaviours in the sample was 33% (n=13) for children diagnosed with Septo-Optic Dysplasia/Optic Nerve Hypoplasia, Physical Aggression (e.g. punching, pushing, kicking, pulling and grabbing) was reported in 85% of the children, 77% of children demonstrated disruption and destruction of property or the environment, and 85% of children exhibited stereotyped behaviours (e.g. rocking, twiddling, and eye pressing and constant hand movements).

The percentage of children showing a specific Self Injurious Behaviour in a repetitive manner (>twice in succession) included 62% of the group, hitting themselves with a body part (slaps head or face) included 38% of children, hitting self against surface or object 31%, hitting self with object was 46%, biting themselves 23% pulling (pulling hair or skin), 46% displayed rubbing or scratching self, and 31% of children inserted their fingers or objects (e.g. eye poking).

Chapter Six, found that the risk markers for Self Injurious Behaviours were the degree of intellectual disability, sensory processing impairments, severity of autistic behaviours, and children's level of visual function. Furthermore, the motivations for Self Injurious Behaviours appeared to be multi-factorial, and included sensory stimulation,

attention, escape and tangible reasons. Previous research has indicated that Self Injurious Behaviours provided children with Sensory stimulation (Edelson, 1984) Maisto *et al.*, (1978), and this was reported on the Motivation Assessment Scale and confirmed by the Short Sensory Profile. However, Sensory Stimulation appeared to be a secondary reason for a motivation towards Self Injurious Behaviours. Children with Septo Optic Dysplasia and Optic Nerve Hypoplasia tended to use Self Injurious Behaviours as a means of communication.

7.4 Evaluation of previous research to present findings

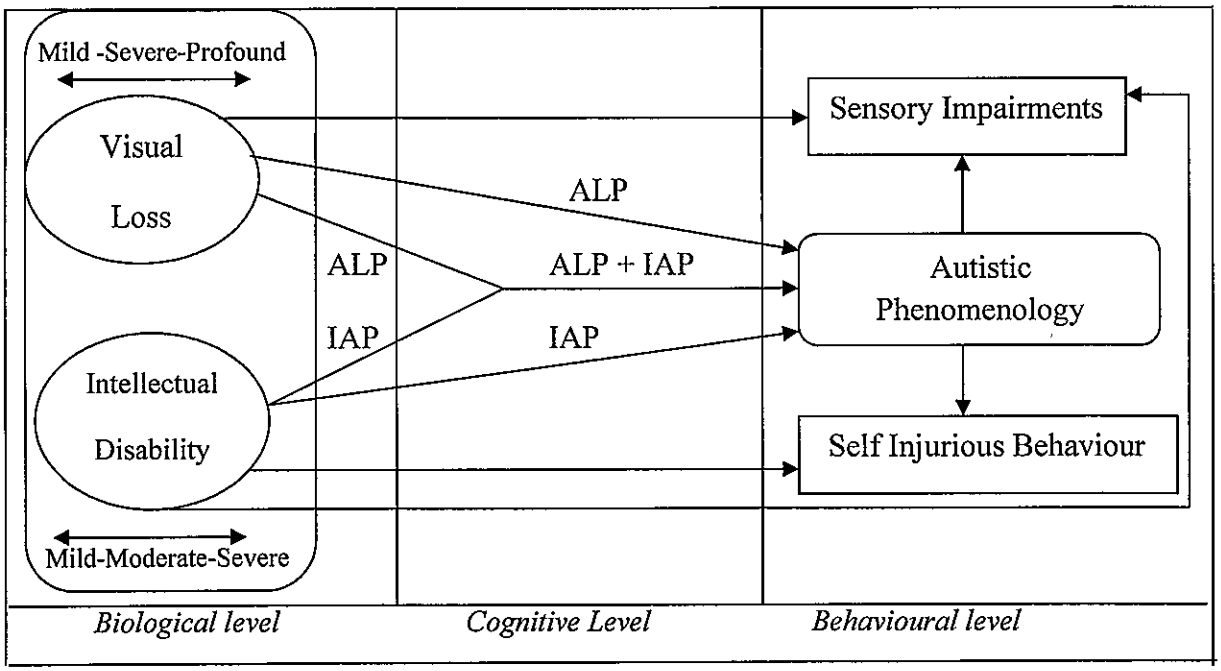
Hobson (2004) suggests, that there is "not a clear boundary between blind children with autism and those with autistic [-like] features" (Hobson, 2005: pg, 15). Some explanations for the over representation of autistic behaviours in the general blind population suggest that blind children acquire autistic phenomenology due to a different pathway, to that of sighted autistic children (Andrews & Wyver 2005). More recently, Brambring, (2008) suggests that autistic behaviours in the blind are better explained as an information acquisition problem, due to visual loss blocking external social and communicative information, and that autism in the sighted autistic children is more likely to be a result of deep developmental delays leading to internal information processing impairments (Brambring, 2008). Therefore, there is a clear distinction between external contributing factors to autistic phenomenology in the blind, and that of internal factors in the sighted autistic children.

Children's unusual responses to sensory inputs have been reported to correlate strongly with Restrictive, Repetitive and Stereotyped behaviours (Rogers, Hepburn, & Wehner, 2003). Some researchers consider Restrictive, Repetitive and Stereotyped behaviours an antecedent of sensory processing disorders (Ornitz, 1989), whereas others

argue that Restrictive, Repetitive and Stereotyped behaviours and sensory processing disorders are co-morbid with one another (Rogers, Hepburn, & Wehner, 2003). For such reasons, some researchers consider Self-Injurious behaviours as a "substrate of stereotyped behaviours" (Gorman-Smith & Matson, 1985).

7.5 Implications of the research

From these observations and previous research, it is likely that autism in children with Optic Nerve Hypoplasia and Septo Optic Dysplasia could be explained by three possible pathways. The Frith, Leslie and Morton casual model of autism (1991) has been adapted to explain the findings of the present study. Figure ten, shows that visual loss and intellectual disability were both contributing factors and possibly interrelated factors, in the occurrence of autistic phenomenology in children with Septo-Optic Dysplasia and Optic Nerve Hypoplasia.



**ALP = Autistic Like Pathway, IAP + Idiopathic Autistic Pathway*

Figure ten: the three pathways to autistic phenomenology, and its associated behaviours in children with Septo Optic Dysplasia and Optic Nerve Hypoplasia.

7.6 The clinical relevance of the findings of the thesis

The clinical relevance of the findings of the thesis is that all children with Septo Optic Dysplasia and Optic Nerve Hypoplasia should have their development closely monitored by paediatric services at the hospital they attend. Dale and Sonsken (2002) state that children experience a critical period, in which developmental regression can occur and it is crucial that this can be identified quickly in order to deliver early intervention.

Furthermore, not being able to isolate the impact of intellectual disability, from that of the impact of visual impairment, can make it difficult to isolate the origin of autism in the blind. The thesis also raises the further possibility that intellectual disability and visual loss may have an accumulative effect to the severity of autistic disorders within the present clinical cohort. Differentiating between transient autistic like behaviours, autistic behaviours which are functionally adaptive for children with severe to profound levels of visual loss and children who have co-morbid autistic disorders due to neurological alterations to the brain, could bring a better understanding to the aetiology of autism in general (Hobson, 2005).

The findings of the empirical Chapters of the thesis demonstrate the importance of early diagnosis and early intervention. However, problems arise in developing a specialised intervention programme for children who are both blind and autistic. Interventions are available for children who are blind, and interventions are available for sighted autistic children, but trying to integrate these two interventions has yet to be accomplished.

7.7 The Limitations of the research studies

In Chapter Three, the limitations of the study were the small sample size and lack of younger children in the cohort. Most importantly, children with varying degrees of visual impairments needed to be matched to autistic children, according to their intellectual ability, age, and gender, but due to difficulties in recruitment, this was not achieved. Children with visual impairments and no associated intellectual impairments more frequently attend mainstream schools, however this group proved to be difficult to access.

A methodological limitation of Chapter Four,, was that diagnosis of visual loss was not received by an ophthalmologist and relied on parental reporting for the severity of visual loss. Due to the low incidence rate of the clinical conditions three charities were approached for the thesis, this lead to the absence of detailed medical records to shed light on children's complete clinical picture. The diagnosis of Optic Nerve Hypoplasia and Septo Optic Dysplasia for children from charities could not be corroborated through medical records which could have resulted in inaccurate clinical group membership. As these two clinical conditions are closely related, further medical testing through the lifespan of the child could mean that clinical diagnosis of these two conditions could have changed over time.

Recruitment biases could have occurred as charities were also approached for recruitment, and this could resulted in a non representative sample. Parents who are members of a charity, or who took part in the research project through the hospital could have participated because they were concerned about their child's behaviours.

Also, it is not known whether early educational interventions may have led to improvements in children's adaptive and cognitive functioning was not known for the present study, and could have impacted the results greatly. More importantly, if

improvements could have been detected, in the adaptive and cognitive profiles of children due to early educational interventions, this would further endorse the importance of early diagnosis of autism, and the influence of early educational interventions.

Differences between the parental reporting of Autistic Spectrum Disorders could have occurred due to parent's understanding and experience of autistic disorders. However, differences in the specific criteria and data collection method used to define Autistic Spectrum Disorder could contribute to the differences between the present theses and that of Parr *et al.*, (2008). For example, the criteria for Autistic Spectrum Disorders over the last thirty years have developed into a spectrum of disorders along a continuum and this could explain the increased occurrence of autism in the present theses.

For the assessment of Restrictive Repetitive and Stereotyped Behaviours and sensory processing disorders there was a reliance on parental reporting through rating scales, and this could have resulted in an over representation of these behaviours. Direct observation of these behaviours was only achieved during the Autism Diagnostic Observation Schedule, which usually takes 30-40 minutes to complete and the duration of this assessment may have been too short, in order to identify Restrictive Repetitive and Stereotyped Behaviours in children. Furthermore, it is not known how age impacted these behaviours and research has demonstrated that Restrictive, Repetitive and Stereotyped behaviours occurs more frequently in younger children (Bodish, 2000).

Due to the uneven group membership, low sample size and violation of normality testing, non parametric tests were utilised. Non parametric tests come with disadvantages such as low power, and low precision. Most importantly, confounding variables could not be controlled for through the use of parametric testing. A further limitation of the study was that further comparison groups were not recruited. Future

research could incorporate a heterogeneous group of children with visual loss, and a group of children with intellectual disabilities. Such as comparison, could further explain whether visual loss or intellectual disability account better for autistic disorders in the present clinical cohort of children.

7.8 Suggestions for future research

Future research would need to examine how joint attention abilities, pointing, gestures and showing are achieved in a large sample of blind children with and without intellectual disability and whether impairments in these areas result in elevated scores on the Autism Diagnostic Observation Schedule. Furthermore, if the developmental path of these behaviours can be mapped in the congenitally blind children and applied to the area of autism and visual impairments this may help to answer questions about the sources of similarities between the two conditions. Future research will need to explore how children acquire information about their social and communicative world from their intact senses compared to how they process this information and this can be achieved through cognitive neuroscience techniques.

The developmental trajectories of children with visual loss and/or autism need to be closely examined through longitudinal research methodologies to establish when these children reach certain developmental milestones and are at risk from specific psychosocial factors. Longitudinal research can also assess whether autistic behaviours in the blind are only surface similarities and transient features (Baron-Cohen, 2002) by following children who have been identified as having autistic disorders in the present cohort and assessing their autistic behaviours over a period of time. Importantly, when explaining autistic symptoms in the visually impaired, the early developmental profiles

and, current levels of intellectual disability and associated impairments need to be carefully observed.

Furthermore, future research needs to look at the results of MRI scans and specifically the role of the corpus collosum, and autistic disorders in children with Septo Optic Dysplasia and Optic Nerve Hypoplasia. The corpus collosum is strongly implicated in autistic disorders and it is either absent or impaired in children in Septo Optic Dysplasia (Manes *et al.*, 1999).

There are a number of validated assessment tools available to measure Restrictive Repetitive and Stereotyped Behaviours. Future research would need to use these tools but with modifications would which would take into consideration children's severe to profound levels of visual loss. Furthermore, direct observations in a number of environmental settings would provide an insight into the triggers for maladaptive behaviours. Future research needs to address whether children with different neurological impairments, display different types of sensory impairments. Furthermore, the study has demonstrated that the intact senses of children with Septo Optic Dysplasia and Optic Nerve Hypoplasia can be greatly affected, and this ultimately influences their expressed behaviours.

It is also important to assess the motivations for Self Injurious Behaviours for each individual child. This would include a functional assessment of the when, where, how often a behaviour occurs and with what intensity a particular Self Injurious Behaviour manifests. From the functional assessment of a child's Self Injurious Behaviours preventative strategies and interventions could be incorporated to reduce Self Injurious Behaviours.

7.9 Overall findings of the thesis

The results of the present study demonstrate that, regardless of the pathway which accounts for autistic phenomenology in children with Septo Optic Dysplasia and Optic Nerve Hypoplasia, these children still require the appropriate educational provisions and early diagnosis of autism.

The lack of appropriate diagnostic tools can lead to diagnostic overshadowing, which can ultimately leave children without the appropriate medical and educational provisions. Reasons for an absence of such a tool, appear to be due to an uncertainty about what is a "typical" development path for a blind child, and that most current assessments rely heavily on impairments in joint attention abilities and eye gaze alterations in their diagnostic criteria. Furthermore, when diagnostic assessments are altered this reduces their psychometric properties. Inadvertently, the study also highlights that the "gold standard" assessments need to be inclusive of all children's disabilities, and this lack of appropriate assessment instruments for autistic disorders leave many children overlooked for the diagnosis of autism.

The present study demonstrates that regardless of the pathway which accounts for autistic phenomenology in children with Septo Optic Dysplasia and Optic Nerve Hypoplasia, these children still require the appropriate educational provisions and early diagnosis of autism. In turn, this may help to differentiate between the transient autistic like behaviours from that of the persistent Kanner (1943) type autism which is often observed in sighted autistic children. However, it is not possible to differentiate between autism and autistic like behaviours until a standardised diagnostic instrument to assess autism in the blind is established. The difficulties of creating such an instrument lie in the low incidence of visual impairments, the heterogeneity of visual loss, its co-morbidity

with intellectual disability, and more importantly trying to find a cohort of children on whom to standardise an assessment.

Acers, T.E. (1981). Optic nerve hypoplasia: septo-optic-pituitary dysplasia syndrome. *Transatlantic American Ophthalmology Society,* 79, 425–457.

Adachi, T., Koeda, S., Hirabayashi, Y., Maeoka, M., Shiota, M., Wright., E.D., & Wada, A. (2004). The metaphor and sarcasm scenario test: a new instrument to help differentiate high functioning pervasive developmental disorder from attention deficit/hyperactivity disorder. *Brain and Development,* 26, (5), 301-306.

Adrien, J. L., Perrot, A., Sauvage, D., Leddet, I., Larmande, C., Hameury, L. & Barthelemy, C. (1992). Early symptoms in autism from family home movies. Evaluation and comparison between 1st and 2nd year of life using I.B.S.E. scale. *Acta Paedopsychiatrica,* 55, 71-75.

Adrien, J.L., Barthélémy, C., Perrot, a., Roux, s., Lenoir, p., Hameury, L., & Sauvage, D. (1992). The Infant Behavioral Summarized Evaluation (IBSE): A Rating Scale for the Assessment of Young Children with Autism and Developmental Disorders, Validity and Reliability', *Journal of Autism and Developmental Disorders* 3: 375–94.

Adrien, J.L., Faure, M., Perrot, A., Hameury, L., Garreau, B., Barthelemy, C., & Sauvage, D. (1991). Autism and family home movies: Preliminary findings. *Journal of Autism and Developmental Disorders*, 21(1), 43-49.

Ahmad, T., Garcia-Filion, P., Borchert, M., Kaufman, F., Burkett, L., & Geffner, M. (2006) Endocrinological and Auxological Abnormalities in Young Children with Optic Nerve Hypoplasia: A Prospective Study. *The Journal of Pediatrics*, 14 (1), 74-85.

Akshoomoff, N., Pierce, K., & Courchesne, E. (2002). The neurobiological basis of autism from a developmental perspective. *Developmental Psychopathology,* 14(3), 613-634.

Altman, D. G., & Bland, J. M. (1994). Statistics Notes: Diagnostic tests 1: sensitivity and specificity. *British Medical Journal,* 308, 1552.

Aman, M. G., & Singh, N. N. (1986). *Aberrant Behaviour Checklist Manual.* East Aurora, NY: Slosson Educational Publications.

American Psychiatric Association. (1980). *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV).* (3rd Ed). Washington, DC: American Psychiatric Association.

American Psychiatric Association. (1994). *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV). (4th Ed).* Washington, DC: American Psychiatric Association.

American Psychiatric Association. (2000). *American Psychiatric Association, Diagnostic and statistical manual of mental disorders (DSM-IV-TR),* Washington, DC: American Psychiatric Association.

Andrews, R. & Wyver, S. (2005). Autistic tendencies: Are there different pathways for blindness and Autism Spectrum Disorders? *British Journal of Visual Impairment*, 23(2), 52-57.

Antonini, S. R. R., Grecco Filho, A., Elias, L. L. K., Moreira, A. C., & Castro, M. (2002). Cerebral midline developmental anomalies: endocrine, neuroradiographic and ophthalmological features. *Journal of pediatric endocrinology & metabolism*, 5(9), 1525-1530.

Arslanian, S. A., Rothfus, W. E., Foley, Jr T. P., & Becker D.J. (1984). Hormonal, metabolic, and neuroradiologic abnormalities associated with septo-optic Dysplasia. *Acta Endocrinologica*, 107(2), 282-288.

Awan, K.J. (1976). Ganglionic neuroretinal aplasia and hypoplasia: aplasia and hypoplasia of optic nerve. *Annals of Ophthalmology*, 8(10), 1193–1202.

Axelrad, M.A., Nicholson, L., Stabley, D.L., Sol-Church, K., & Gripp, K.W. (2007). Longitudinal assessment of cognitive characteristics in Costello syndrome. *American Journal of Medical Genetics Part A*, 143A (24), 3185-3193.

Bahar, C., Brody, J., McCann, M.E., Mendiola, R.M. & Slott, G. (2003) 'A multidisciplinary approach to educating preschool children with optic nerve hypoplasia and septo-optic nerve dysplasia', *RE:view*, 35(1), 15–21.

Bailey, A., Le Couteur, A., Gottesman, I., Bolton, P., Simonoff, E., Yuzda, E., & Rutter, M (1995). Autism as a strongly genetic disorder: evidence from a British twin study. *Psychological Medicine*, 25(1), 63-67.

Bailey, A., Luthert, P., Dean, A., Harding, B., Janota, I., Montgomery, M., Rutter, M., & Lantos, P. A. (1998). Clinicopathological study of autism. *Brain*, 121(5), 889–905.

Baird, G., & Charman, T. (2002). Practitioner Review: Diagnosis of autism spectrum disorder in 2- and 3-year-old children. *Journal of Child Psychology and Psychiatry,* 43 (3), 289 – 305.

Baird, G., Charman, T., Baron-Cohen, S., Cox, A., Swettenham, J., Wheelwright, S., & Drew, A. (2000). A screening instrument for autism at 18 month of age: A six-year follow-up study. *Journal of the American Academy of Child and Adolescent Psychiatry,* 39, 694–702.

Baird, G., Simonoff, E., Pickles, A., Chandler, S., Loucas, T., Meldrum, D., & Charman, T. (2006). Prevalence of disorders of the autism spectrum in a population cohort of children in South Thames: the Special Needs and Autism Project (SNAP). *Lancet*, 368, 210–15.

Bak, S. (1999) 'Relationships between inappropriate behaviours and other factors in young children with Leber's Congenital Amaurosis. *Developmental Medicine and Child* children with visual impairments. *RE:view,* 31(2), 84-91.

Baker, A.E., Lane, A., Angley, M.T., & Young, R.L. (2007). The relationship between sensory processing patterns and behavioural responsiveness in autistic disorder: A pilot study. *Journal of Autism and Developmental Disorders,* 35(8), 867-875.

Baranek, G. T. (1999). Autism during infancy: a retrospective video analysis of sensory-motor and social behaviours at 9-12 months of age. *Journal of Autism and Developmental Disorders,* 29, 213-224.

Baranek, G.T. (2006). Sensory Experiences Questionnaire: discriminating sensory features in young children with autism, developmental delays, and typical development. *Journal of Child Psychology and Psychiatry*, 47(6), 591-601.

Bartek, L., & Rutter, M. (1976). Differences between mentally retarded and normally intelligent autistic children. *Journal of Autism and Childhood Schizophrenia, 6,* 109–120.

Barkovich, A.J., Fram, E.K. & Norman, D. (1989). Septo-optic dysplasia: MR imaging. *Radiology*, 171, 189-192.

Baron-Cohen, S. (1989b). The autistic child's theory of mind: a case of specific developmental delay. *Journal of Child Psychology and Psychiatry*, 30, 285-298.

Baron-Cohen, S. (2002). I am loved, therefore I think. *Nature,* 416, 791 – 792.

Baron-Cohen, S., Leslie, A.M., & Frith, U. (1985). Does the autistic child have a `theory of mind'? *Cognition*, 21, 37-46.

Baron-Cohen, S., Allen, J. Gillberg, C. (1992) Can Autism be detected at 18 months? British Journal of Psychiatry, 161, 839-843.

Baron-Cohen, S., & Goodhart, F. (1994). The "seeing leads to knowing" deficit in autism: the Pratt and Bryant probe. *British Journal of Developmental Psychology*, 12, 397-402.

Barrett, S., Beck, J.C., Bernier, R., Bisson, E., Braun, T.A., Casavant, T.L., Childress, D., et al. (1999). An autosomal genomic screen for autism. *American Journal of Medical Genetics,* 88, 609-615.

Bartak, L., & Rutter, M., (1976). Differences between mentally retarded and normally intelligent autistic children. *Journal of Autism and Developmental Disorders*, 6(2), 109 - 120.

Baumeister, A. A. (1978). Origins and control of stereotyped movements. In C. E. Meyers (Ed.), *Quality of life in severely and profoundly mentally retarded people: Research foundations for improvement* (pp. 353–384). Washington, DC: American Association on Mental Deficiency Monograph, No. 3.

Baumeister, A.A., & Rollings, J.P. (1976). Self-injurious behavior. In N.R. Ellis (Ed.), *International review in mental retardation (Vol. 9).* New York: Academic Press.

Baxter, L. R. (1992). Neuroimaging studies of obsessive compulsive disorder. In: M. A. Jenike, Editor, *Psychiatric clinics of North America: Obsessional disorders*, Saunders, Philadelphia, pp. 871–884.

Benner, J.D., Preslan, M.W., Gratz, E., Joslyn, J., Schwartz, M., & Kelman, S. (1990). Septo-optic dysplasia in two siblings. *American Journal of Ophthalmology*, 109, 632–637.

Bennetto, L; Pennington, B; Rogers, S. (1996). Intact and impaired memory functions in autism. *Child Development,* 67, 1816–1835.

Ben-Sasson, A., Hen, L., Fluss, R., Cermak, S.A., Engel-Yeger, E., (2009). "A meta-analysis of sensory modulation symptoms in individuals with autism spectrum disorders. *Journal of Autism Developmental Disorders,* 39(1), 1-11.

Berkson, G. (1996). Feedback and control in the development of abnormal stereotyped behaviors. In R. L. Sprague, & K. M. Newell (Eds.), *Stereotyped movements Brain and behaviour relationships*. Washington, DC: American Psychological Association.

Berument, S. K., Rutter, M., Lord, C., Pickles, A., & Bailey, A. (1999) Autism screening questionnaire: diagnostic validity. *British Journal of Psychiatry*, 175, 444-451.

Beshyah, S.A., Henderson, A., Niththyananthan, R., Skinner, E., Anyaoku, V., Richmond, W., Sharp, P., & Johnston, D.G. (1995). The effects of short and long-term growth hormone replacement therapy in hypopituitary adults on lipid metabolism and carbohydrate tolerance. *Journal of Clinical Endocrinology and Metabolism*, 80(2), 356-63.

Beshyah, S.A., Shahi, M., Skinner, E., Sharp, P., Foale, R., & Johnston, D.G. (1994). Cardiovascular effects of growth hormone replacement therapy in hypopituitary adults. *European Journal of Endocrinology*, 130(5), 451-458.

Bigelow, A. (2003) 'The Development of Joint Attention in Blind Infants. *Development and Psychopathology* 15: 259–75.

Billson, F.A. (1973). The clinical significance of optic nerve Hypoplasia. *Transactions of the Ophthalmological Society of New Zealand*, 25, 179–180.

Birkabaek, N.H., Patel, L., Wright, N.B., Grigg, J. R., Sinha, S., Hall, C. M., Price, Lloyd, D. A., & Clayton, P. E. (2003) Endocrine status in patients with optic nerve hypoplasia: Relationship to midline central nervous system abnormalities and appearance of the hypothalamic-pituitary axis on magnetic resonance imaging. *Journal of Clinical Endocrinology and Metabolism*, 88 (11), 5281 –5286.

Bishop M, Hobson P., & Lee A. (2005) Symbolic play in congenitally blind children. *Developmental and Psychopathology*, 17(2), 447-465.

Bishop, D.V.M. & Norbury, C.F. (2002) Exploring the borderlands of autistic disorder and Specific language impairment: A study using standardised diagnostic instruments. *Journal of Child Psychology and Psychiatry*, 43, 917-929.

Blethen, S.L., & Weldon, V.V.(1990) Hypopituitarism and septo-optic dysplasia in first cousins. *American Journal of Ophthalmology*, 109, 632-7 52.

Blohmé, J., Bengtsson-Stigmar E., & Tornqvist, K. (2001). Visually impaired Swedish children. Longitudinal comparisons 1980–1999. *Acta Ophthalmologica Scandinavica* 78(4), 416 – 420.

Bodfish, J.W., Crawford, T.W., Powell, S.B., Parker, D.E., Golden, R.N., & Lewis, M.H. (1995). Compulsions in adults with mental retardation: Prevalence, phenomenology, and comorbidity with stereotypy and self-injury. *American Journal of Mental Retardation*, 100, 183-192.

Bodfish, J.W. (1995). Stereotypy in behavioral & psychiatric disorders: A new understanding, a new technology of treatment. Clinical Update 1995. *Western Carolina Center Research Report.*

Bodfish, J.W., Symons, F.J., Parker, D.E., & Lewis, M.H. (2000) Varieties of repetitive behavior in autism: Comparison to mental retardation. *Journal of Autism and Developmental Disabilities*, 30, 237-243.

Bodfish, J. W., Symons, F. J., & Lewis, M. H. (1999). The Repetitive Behavior Scale. Western Carolina Center Research Reports.

Bogdashina, O. (2003). *Sensory perceptual issues in autism and Asperger Syndrome: different sensory experiences – different perceptual worlds.* London: Jessica Kingsley Publishers.

Boger-Megiddo, I., Shaw, D.W.W., Friedman, S.D., Sparks, B.F., Artru, A.A., Giedd, J.N., Dawson, G., & Dager, S.D. (2006) Corpus callosum morphometrics in young children with autism spectrum disorder. *Journal of Autism and Developmental Disorders*, 36 (6), 733 –739.

Bolte, S., & Poutska, F. (2003). The Recognition of Facial Affect in Autistic and Schizophrenic Subjects and Their First-Degree Relatives. *Psychological Medicine,* 33 (5), 907–915.

Bonati, M.T. Bonati, S. Russo, P. Finelli, M.R. Valsecchi, F. Cogliati, F. Cavalleri, W. Roberts, M. Elia and L. Larizza. (2007). Evaluation of autism traits in Angelman syndrome: a resource to unfold autism genes, *Neurogenetics* 8, 169–178.

Boucher, J. (1999). Editorial: interventions with children with autism methods based on play. *Child Language Teaching and Therapy*, 15 (1), 1-5.

Brambring, M. (1998). *Lessons with a child who is blind. Development and early intervention in the first years of life.* Okemos, MI: Blind Children's Fund.

Brambring, M., & Tröster, H. (1992). On the stability of stereotyped behaviors in blind infants and preschoolers. *Journal of Visual Impairment & Blindness, 35,* 775-78.

Brambring, M., (2008) Behaviour *Problems in Children and Adolescents with Visual Impairment.* Retrieved 6, December, 2008, From, http://www.icevieurope.org/cracow2000/proceedings/chapter06/06-04.doc

Brodsky, M.C. (1991) Septo-optic dysplasia: a reappraisal. *Seminars in Ophthalmology*, 6, 227-232.

Brodsky, M.C., & Glasier, C.M. (1993). Optic nerve hypoplasia. Clinical significance of associated central nervous system abnormalities on magnetic resonance imaging. *Archives of Ophthalmology*, 111 (1), 66 –74.

Brodsky, M.C., Baker, R.S., & Hamed, L.M. (1996). Pediatric Neuroophthalmology. New York, Springer- Verlag.

Brodsky, M.C., Conte, F.A., Taylor, D., Hoyt, C.S., & Mrak, R.E. (1997). Sudden death in septo-optic dysplasia: report of 5 cases. *Archives of Ophthalmology*, 115, 66-70.

Brook, C.G.D., Sanders, M.D., & Hoare, R.D. (1972). Septo-optic dysplasia. *British Medical Journal,* 3, 811-813.

Brown, K. Rodgers, J. Johnstone, H. Adams, W. Clarke, M. Gibson, M. & Cheetham, T. (2004). Abnormal cognitive function in treated congenital hypopituitarism. *Archive of Diseases in Childhood*, 89(9), 827–830.

Brown, R. Hobson, R.P., Lee, A. & Stevenson, J. (1997) 'Are There 'Autistic Like' Features in Congenitally Blind Children?' *Journal of Child Psychology and Psychiatry* 38: 693–703.

Bruininks, R., Woodcock, R., Weatherman, R., & Hill, B. (1996). *Scales of Independent Behaviour - Revised.* Park Allen, TX: DLM Teaching Resources.

Bulla, N. (2002). *Evaluating children with visual impairments for eligibility in talented and gifted programs.* Retrieved august 5, 2007, from Texas School for the Blind and Visually Impaired Web site: http://www.tsbvi.edu/Education/testing.html.

Burack, J. A., & Volkmar, F. R. (1992). Development in high- and low-functioning autistic children. Journal of Child Psychology and Psychiatry, 33, 607-616.

Burlingham, D. (1965) Some problems of ego development in blind children. *Psychoanalytic Study of the Child*, 20, 194–208.

Campbell, M., Locascio, .J, Choroco, B., *et al.* (1990). Stereotypies and tardive dyskinesia: Abnormal movements in autistic children. *Psychopharmalogical Bulletin*, 26, 260–266.

Carpentieri, S., & Morgan, S. (1996). Adaptive and Intellectual Functioning in Autistic and Non-Autistic Retarded Children. *Journal of Autism and Developmental Disorders,* 26, 611–20.

Carr, E. G., Newsom, C. D., & Binkoff, J. A. (1976). Stimulus control of self-destructive behavior in a psychotic child. *Journal of Abnormal Child Psychology*, 4,139-152.

Carter, A., Volkmar, F., Sparrow, S., Wang, J., Lord, C., Dawson, G., Fombonne, E., Loveland, K., Mesibov, G., & Schopler, E. (1998). The Vineland Adaptive Behavior Scales: Supplementary norms for individuals with autism. *Journal of Autism and Developmental Disorders, 28,* 287–302.

Carvalho, L.R., Woods, K.S., Mendonca, B.B., Marcal, N., Zamparini, A.L., Stifani, S. Brickman, J.M., Arnhold, I.J.P, & Dattani, M.T. (2003). A homozygous mutation in HESX1 is associated with evolving hypopituitarism due to impaired repressor-corepressor interaction. *Journal of Clinical Investment*, 15, 112(8), 1192–1201.

Carvill, S., & Marston, G. (2002) People with Intellectual Disability, Sensory Impairments and Behaviour disorder, a case series. *Journal of Intellectual Disability Research*, 46. (3), 264- 272.

Cass, H. (1996) Autism and visual impairment - what we know about causation and early identification. Proceedings of the Autism and Visual Impairment Conference. Sydney.

Cass, H. (1998).Visual Impairment and Autism: Current Questions and Future. *Autism*, 2:117-138.

Cass, H., Sonsken, P.M., & McConachie, H.R. (1994) Developmental Setback in Severe Visual Impairment. *Archives of Disease in Childhood* 70,192–6.

Cath, D.C., Spinhoven P., Hoogduin, C. A. L Andrea, Landman, D., van Woerkom, T. C. A. M., van de Wetering, B J. M., Roos, R. A. C., & Rooijmans, H. G. M. (2001). Repetitive behaviors in Tourette's syndrome and OCD with and without tics: what are the differences? *Psychiatry Research*, 101, (2), 171-185.

Celeste, M. (2006). Play Behaviors and Social Interactions of a Child Who Is Blind: In Theory and Practice. *Journal of Visual Impairment & Blindness*, 100(2), 521-533.

Chakrabarti, S., & Fombonne, E. (2001). Pervasive developmental disorders in preschool children. *Journal of the American Medical Association*, 285, 3093–3099.

Chan, C. C., Fishman, M., & Egbert, P. R., (1978). Multiple ocular anomalies associated with maternal LSD ingestion. *Archives of Ophthalmology*, 96, 282-284.

Charman, T., Swettenham, J., Baron-Cohen, S., Cox, A., Baird, G., & Drew, A. (1998). An experimental investigation of social cognitive abilities in infants with autism: Clinical implications, *Infant Mental Health Journal*, 19, 260–275.

Chase, J.B. (1972). *Retrolental Fibroplasia and Autistic Symptomatology.* American Foundation for the Blind: New York.

Chess, S., Fernandez, P., & Korn, S.J. (1978). Behavioural consequences of congenital rubella. *Paediatrics*, 93(4), 699-703.

Clayton, R.N. (1998). Mortality, cardiovascular events and risk factors in Hypopituitarism. *Growth Hormone and IGF Research*, 8(A), 69-76.

Cohen, I.L. (2003). Criterion-related validity of the PDD Behavior Inventory, *Journal of Autism and Developmental Disorders,* 33, 47–53.

Cohen, R.N., Cohen, L.E., Botero, D., Yu, C., Sagar, A., Jurkiewicz, M., & Radovick, S. (2003). Enhanced repression by *HESX1* as a cause of hypopituitarism and septooptic dysplasia. *Journal of Clinical Endocrinology and Metabolism*, *88*, 4832–4839.

Constantino, J. N., Davis, S. A., Todd, R. D., Schindler, M. K., Gross, M. M., Brophy, S. L., et al. (2003).Validation of a brief qualitative measure of autistic traits: Comparison of the social responsiveness scale with the Autism Diagnostic Interview-Revised. *Journal of Autism and Developmental Disorders*, 33, 427–433.

Conti-Ramsden, G.M., Simkin, Z., Botting, N.F. (2006). The prevalence of autistic spectrum disorders in adolescents with a history of specific language impairment (SLI). *Journal of Child Psychology and Psychiatry*, 47(6), 621-628.

Costin, G., & Murphree, A. L. (1985) Hypothalamic-pituitary function in children with optic nerve hypoplasia. *American Journal of Diseases in Childhood*, 139(3), 249-54.

Cunningham, A., & Schreibman, L. (2007). Stereotypy in Autism: The Importance of Function. *Research in Autism Spectrum Disorders*, 2(3), 469–479.

Curcio, F. (1978). Sensorimotor functioning and communication in mute autistic children. *Journal of Autism and Childhood Schizophrenia*, 8, 281–291.

Dale, N. & Sonksen, P. (2002). Developmental Outcome, Including Setback, in Young Children with Severe Visual Impairment. *Developmental Medicine & Child Neurology*, 44, 613-622.

Dale, N. (2005). Early signs of developmental setback and autism in infants with severe visual impairments. In Pring (Ed) *Autism and Blindness: Research and Reflections*. Whurr Publishers, London

Dale. N., & Salt, A. (2008). Social Identity, Autism and Visual Impairment (VI) in the early years. *British Journal of Visual Impairment*, 26, (2), 135-146.

Damasio, A. R. & Maurer, R. G. (1978). A neurological model for childhood autism. *Archives of Neurology*, 35, 777–786.

Dattani, M. T., Martinez-Barbera, J. P., Thomas, P. Q., Brickman, J. M., Gupta, R., Wales, J. K., Hindmarsh, P. C., Beddington, R. S. & Robinson, I. C. (1999). HESX1: a novel gene implicated in a familial form of septo-optic dysplasia. *Acta Paediatrics.* 88, 49-54.

Dattani, M.T. (2005). Growth hormone deficiency and combined pituitary hormone deficiency: does the genotype matter? *Clinical Endocrinology*, 63(2).121-30.

Dattani, M.T., & Robinson, I.C. (2000). The molecular basis for developmental disorders of the pituitary gland in man. *Clinical Genetics.* 57(5), 337– 346.

Dattani, M.T., & Robinson, I.C. HESX1 and Septo-Optic Dysplasia. (2000). *Reviews in endocrine & metabolic disorders,* 3(4) 289-300.

Dattani, M.T., Martinez-Barbera, J.P., Thomas, P.Q., Brickman, J.M., Gupta, R., Martensson, I.L., Toresson, H., Fox, M., Wales, J.K.H., Hindmarsh, P.C., Krauss, S., Beddington, R.S.P., & Robinson, I.C.(1998).. Mutations in the homeobox gene *HESX1/Hesx1* associated with septo-optic dysplasia in human and mouse. *Nature Genetics*, 19 125–133.

David, A., Wacharasindhu., A., & W.A. Lishman. (1993). Severe psychiatric disturbance and abnormalities of the corpus callosum: Review and case series, *Journal of Neurology, Neurosurgery, and Psychiatry,* 56, 85–93.

Delacato. C. H. (1974). *The ultimate stranger - the autistic child.* USA: Arena Press

De Giacomo, A., & Fombonne, E. (1998). Parental recognition of developmental abnormalities in autism. *European Journal of Child and Adolescent Psychiatry*, 7, 131-136.

de Lissovoy, V. (1963). Head banging in early childhood: a suggested cause. *The Journal of Genetic Psychology, 102,* 109-114.

De Meyer, M.K. (1976). Motor, perceptual-motor and intellectual disabilities of communication deficits associated with the spectrum of autism. *Journal of Autism and Developmental Disorders,* 30, 205-23.

De Morsier, G. (1956). Studies on malformation of cranioencephalic sutures. III. Agenesis of the septum lucidum with malformation of the optic tract. *Schweizer Archiv für Neurologie und Psychiatrie,* 77 (1–2), 267 –292.

Deiner, M.S., Kennedy, T.E., Fazeli, A., Serafini, T., Tessier-Lavigne, M., & Sretavan, D,W. (1997). Netrin-1 and DCC mediate axon guidance locally at the optic disc: loss of function leads to optic nerve hypoplasia, *Neuron,* 19(3), 575-589.

Dennis M. (1991). Frontal lobe function in childhood and adolescence: A heuristic for assessing attention regulation, executive control, and the intentional states important for social discourse. *Developmental Neuropsychology.*7, 327–358.

Dieterich, E., Steveling, A., & Lukas, A., Seyfeddinipur, N., & Spranger, J. (1980). Congenital anomalies in children of epileptic mothers and fathers. *Neuropediatrics* ,11(3), 274-83.

DiLalla, D. L., & Rogers, S. J. (1994) Domains of the Childhood Autism Rating Scale: Relevance for diagnosis and treatment. *Journal of Autism and Developmental Disorders, 24,* 115–128.

DiLavore, P.C., Lord, C., & Rutter, M. (1995). The Pre-Linguistic Autism Diagnostic Observation Schedule. *Journal of Autism and Developmental Disorders, 25*(4), 355-379.

Dimitropoulos A, & Schultz, R.T. (2009) Autistic-like symptomatology in Prader-Willi syndrome: a review of recent findings. *Current Psychiatry Report,* 9, 159–164.

Dollard, J., Doob, L. W., Miller, N. E. Mowrer, O. H., & Sears. R. R. (1939). Frustration and aggression. New Haven: Yale Univ. Press.

Dominick, K.C., Davis, N.O., Lainhart, J., Tager-Flusberg, H., & Folstein, S (2007). Atypical behaviors in children with autism and children with a history of language impairment. *Research into Developmental Disabilities,* 28 (2), 145–62.

Donahue, S.P., Lavina, A., & Najjar, J. (2005). Infantile infection and diabetes insipidus in children with optic nerve hypoplasia. *British Journal of Ophthalmology,* 89, 1275-1277.

Dunn, W., (1999). *Sensory Profile.* San Antonio, TX:The Psychological Corporation.

Durand V.M & Carr, E.G. (1987). Social influences on 'self-stimulatory' behavior and analysis treatment application. *Journal of Applied Behavioural Analysis,* 20,119–132.

Durand, V.M., & Crimmins, D.B. (1988). Identifying the variables maintaining self-injurious behavior. *Journal of Autism and Developmental Disorders* .18(1):99–117.

Dykens, E.M., Hodapp, R.M., & Leckman, J. (1994). *Behavior and development in fragile X syndrome.* Newbury Park, CA: Sage .

Dykens, E.M., Hodapp, R.M., Walsh, K., & Nash, L.J. (1992). Adaptive and maladaptive behavior in Prader-Willi syndrome. *Journal of the American Academy of Child and Adolescent Psychiatry*, 31, 1131-1136.

Dykens, EM. (2000). Psychopathology in children with intellectual disability. *Journal of Child Psychology and Psychiatry,* 41(4), 407-17.

Eaves, R. C., & Milner, B. (1993). The criterion-related validity of the Childhood Autism Rating Scale and the Autism Behavior Checklist. *Journal of Abnormal Child Psychology, 21*, 481–491.

Edelson, S. M., Taubman, M. T., & Lovaas, O. I. (1983). Some social contexts of self-destructive behavior. *Journal of Abnormal Child Psychology, 11,* 299-312.

Edelson, S.M. (1984). Implications of sensory stimulation in self-destructive behavior. *American Journal of Mental Deficiency, 89,* 140-145.

Edwards, W.C., & Layden, W.E. (1970). Optic nerve hypoplasia. *American Journal of Ophthalmology,* 70(6), 950–959.

Egaas, B., Courchesne, E., & Saitoh, O. (1995). Reduced Size of Corpus Callosum in Autism. *Archives of Neurology.* 52 (8), 794-801

Eisenmajer, R., Prior, M., Leekam, S., Wing, L., Ong, B., Gould, J., & Welham, M. (1998). Delayed Language Onset as a Predictor of Clinical Symptoms in Pervasive Developmental Disorders. *Journal of autism and developmental disorders*, 28(6), 527-534.

Ek, U., Fernell, E., & Jacobson, L. (2005). Cognitive and behavioural characteristics in blind children with bilateral optic nerve hypoplasia. *Acta Paediatics*, 94 (10), 1421 –1426.

Emerson L., Warszawiak. D., de Carvalho Neto, A., Benites Filho, P.R., Bruck, I., & Antoniuk S. (2003). Septo-optic dysplasia plus: case report. *Arquivos de Neuro-Psiquiatria*, 61(3A), 671-676.

Emerson, E. (1992). Self-Injurious Behaviour: An Overview of Recent Trends in Epidemiological and Behavioural Research, *Mental Handicap Research* 5, 49-81.

Emerson, E. (2001). *Challenging Behaviour: Analysis and Intervention in People with Intellectual Disabilitie.s* (2nd Edition). Cambridge: Cambridge University Press

Evans, W.E., & Gray, F.E. (2000). Compulsive-like Behavior in Individuals with Down Syndrome: Its Relation to Mental Age Level, Adaptive and Maladaptive Behavior. *Child Development*, 71(2), 288-300.

Farzin, F., Perry, H., Hessl, D., Loesch, D., Cohen, J., Bacalman, S., & *et al.* (2006). Autism spectrum disorders and attention-deficit/hyperactivity disorder in boys with the fragile X premutation. *Journal of Developmental Behavioural Paediatrics, 27*(2), 137-144.

Fazzi, E., Lanners, J., Danova, S., Ferrarri-Ginevra, O., Gheza, C., Luparia, A., Balottin, U., & Lanzi, G. (1999) Stereotyped behaviours in blind children. *Brain and Development.* 21(8), 522-528.

Fazzi, E., Rossi, M., Signorini, S., Bianchi, P.E., & Lanzi,G. (2007). Leber's congenital amaurois: Is there an autistic component? *Developmental Medicine and Child Neurology* 49, 503–507.

Ferrell, K. A. (1998*). Project PRISM: A longitudinal study of developmental patterns of children who are visually impaired.* Greeley, CO: University of Northern Colorado.

Fielder, A.R., Levene, M.I., Trounce, J.Q., & Tanner, M.S. (1986). *Optic nerve hypoplasia in infancy*. Journal of the Royal Society of Medicine, 79(1), 25-29.

Filipek, P.A., Accardo, P.J., Baranek, G.T, Cook, E.H., Dawson, G., Gordon, B., Gravel, J.S., Johnson C.P., Kellen, R.J., Lev,y S.E., Minshew, N.J., Prizant, B.M., Rapin, I., Rogers, S.J., Stone, W.L, Teplin, S., Tuchman, R.F., & Volkmar, F.R. (1999). The screening and diagnosis of autistic spectrum disorders. Journal of Autism and Developmental Disorders, 29 (6), 439–484

Flavell, J. H., Green, F. L., & Flavell, E. R. (1986). Development of knowledge about the appearance-reality distinction. *Monographs of the Society for Research in Child Development,* 51, 1-87.

Fombonne, E. (2001). Is there an epidemic of autism? *Paediatrics* 107,411-413.

Forehand, R., & Baumeister, A.A. (1971). Rate of stereotyped body rocking of severe retardates as a function of frustration of goal-directed behaviour. *Journal of Abnormal Psychology*, 78(1):35-42.

Foroozan, R. (2005). Superior segmental optic nerve hypoplasia and diabetes mellitus. *Journal of Diabetes Complications*, 19, 165–167.

Fraiberg, S. (1977). *Insights from the blind: Comparative studies of blind and sighted infants*. New York: New American Library.

Friede, R.L. (1989). *Developmental Neuropathology*, (2nd edition). New York: Springer-Verlag.

Frisch, H., Häusler, G., Lindenbauer, S., & Singer, S. (1990). Psychological aspects in children and adolescents with hypopituitarism. *Acta Paediatrics Scandinavia*, 79(6-7), 644-51.

Frisén, L., & Holmegaard, L. (1978). Spectrum of optic nerve hypoplasia. *British Journal of Ophthalmology,* 62(1), 7–15.

Frith, U. (1989). Autism and "Theory of Mind". In C. Gillberg (Ed.), Diagnosis and Treatment of Autism. (pp. 33-52). New York: Plenum Press.

Frith, U. (1991). *Autism and Asperger Syndrome.* New York: Cambridge University Press.

Frith, U. (2003). Autism: Explaining the enigma (2nd edition), Blackwell, Oxford

Frith, U., Morton, J., & Leslie, A.M. (1991). The cognitive basis of a biological disorder: autism. Trends in Neurosciences, 14, 433-438.

Fujisawa, I., Kikuchi, K., Nishimura, K., Togashi, K., Itoh, K., Noma, S., Minami, S., Sagoh, T., Hiraoka, T., Momoi, T., & *et al.*, (1987). Transection of the pituitary stalk: development of an ectopic posterior lobe assessed with MR imaging. *Radiology*, 165(2), 487-489.

Fujita, K., Matsuo, N., Mori, O., *et al.* (1992). The association of Hypopituitarism with small pituitary, invisible pituitary stalk, type 1 Arnold-Chiari malformation, and syringomyelia in seven patients born in breech position: a further proof on birth injury theory on the pathogenesis of "idiopathic" Hypopituitarism. *European Journal of Paediatrics,* 151, 266–270..

Gal, E. (2006). *An investigation of the relationship of sensory differences and intellectual level to stereotyped and self-injurious movements in children.* Unpublished doctoral thesis, Curtin University of Technology, Perth, Western Australia.

Gal, E., Dyck, M., & Passmore A. (2009). The relationship between stereotyped movements and self-injurious behavior in children with developmental or sensory disabilities. *Research in Developmental Disabilities*, 30, 342-352.

Garcia-Filion, P., Epport, K., Nelson, M., Azen, C., Geffner, M.E., Fink, C., & Borchert, M. (208). Neuroradiographic, Endocrinologic, and Ophthalmic Correlates of Adverse Developmental Outcomes in Children with Optic Nerve Hypoplasia: A Prospective sydudy. *Paediatrics*, 121 (3), 653-659.

Gasparetto, E.L., Warszawiak, D., de Carvalho-Neto, A., Benites-Filho, P.R., Bruck, I., & Antoniuk, S. (2003). Septo-Optic Dysplasia plus: case report. *Arq Neuropsiquiatr*. 61(3), 671-676.

Gedye, A. (1989). Extreme self-injury attributed to frontal lobe seizures. *American Journal on Mental Retardation, 94,* 20-26.

Gedye, A. (1992). Anatomy of self-injurious, stereotypic, and aggressive movements: evidence for involuntary explanation. *Journal of Clinical Psychology, 48,* 766-778.

Geffner, M.E. (2002). Hypopituitarism in Childhood. *Cancer Control*, 9(3), 212-22.

Gense, M H., & Gense, J. D. (2005) *Autism Spectrum Disorders and Visual Impairment: Meeting Students' Learning Needs*. New York, NY: American Foundation for the Blind.

Gense, M.H. & Gense, D.J. (2002) Autism Spectrum Disorder in Learners with Blindness/Visual Impairments. Washington, DC: Heldref Publications.

Gernsbacher, M.A., Dawson, M., & Goldsmith, H.H. (2005). Three reasons not to believe in an autism epidemic. *Current Directions in Psychological Science*, 14, 55–58.

Gerstadt, C. L., Hong, Y. J., & Diamond, A. (1994). The relationship between cognition and action: performance of children 3 ½ - 7 years old on a Stroop-like day-night test, *Cognition, 53,* 129-153.

Gillberg, C., Ehlers, S., Schaumann, H., Jakobsson, G., Dahlgren, S. O., Lindblom, .R., Bågenholm, A., Tjuus, T., & Blidner, E. (1990). Autism under age 3 years: a clinical study of 28 cases referred for autistic symptoms in infancy. *Journal of Child Psychology and Psychiatry*, 31, 921-934.

Gillberg, I.C., Gillberg, C., Kopp, S. (1992). Hypothyroidism and autism spectrum disorders. *Journal of Child Psychology Psychiatry*, 33(3), 531-42.

Gillberg C, Rasmussen P (1994), Brief report: four case histories and a literature review of Williams syndrome and autistic behavior. *Journal of Autism Developmental Disorders*, 24, 381-393.

Gillham, J.E., Carter, A.S., Volkmar, F.R., & Sparrow, S.S. (2000). Toward a developmental operational definition of autism. *Journal of Autism and Developmental Disorders, 30,* 269-278.

Gilliam, J.E. (1995). *Gilliam Autism Rating Scale (GARS).* Austin, TX: Pro-Ed

Gillingham, G. 1995. Autism: Fragile Handle With Care. Future Education Inc., 422 E. Lamar Blvd., Suite 106, Arlington, Texas, 76011, U.S.A.

Gingell, K., Parmar, R., Sungum-Paliwal, S. (1996) Autism and multiple pituitary deficiency. *Developmental Medical Child Neurology*, 38(6), 545-549.

Glasson, E.J., et al (2004) Perinatal factors and the development of autism: a population study. *Archives of general psychiatry,* 61, 618-627.

Goldstein, H. (2000). Commentary: Interventions to facilitate auditory, visual and motor integration: "Show me the data." *Journal of Autism and Developmental Disorders*, 30, 423 – 425.

Goodman, R., & Minne, C. (1995). Questionnaire screening for comorbid pervasive developmental disorders in congenitally blind children: A pilot study. *Journal of Autism and Developmental Disorders, 25(2),* 195-203.

Götherström, G., Svensson, J., Koranyi, J., Alpsten, M., Bosaeus, I., Bengtsson, B., & Johannsson G. (2001). A prospective study of 5 years of GH replacement therapy in GH-deficient adults: sustained effects on body composition, bone mass, and metabolic indices. *Journal of Clinical Endocrinology and Metabolism*, 86(10), 4657-65.

Grandin, T. & Scariano, M, (1986). *Emergence: labeled autistic.* Novato, CA: Arena

Grandin, T. (2000). *Thinking in pictures.* New York: Doubleday.

Gray, K.M., Tonge, B.J., Sweeney, D.J., & Einfeld, S.L. (2008). Screening for autism in

young children with developmental delay : an evaluation of the developmental behaviour checklist : early screen. *Journal of Autism and Developmental Disorders* 38(6), 1003-1010

Greenspan, F., & Gardner, D. (2004). *Basic & clinical endocrinology* (7th ed), McGraw-Hill, USA

Goldstein, S., &. Reynolds, C. R. (1985). Handbook of neurodevelopmental and genetic disorders in children. New York: Guilford .

Gorman-Smith, D., & Matson, J.L. (1985). A review of treatment research for self-injurious and stereotyped responding. *Journal of Mental Deficiency Research, 29, 4,* 295-308.

Grossman, A., Savage, M.O., Wass, J.A., Lytras, N., Sueiras-Diaz, J., Coy, D.H., & Besser, G.M. (1983). Growth-hormone-releasing factor in growth hormone deficiency: demonstration of a hypothalamic defect in growth hormone release. *Lancet*, 16; 2 (8342), 137-138.

Gualtieri, C.T. (1989). The differential diagnosis of self-injurious behavior in mentally retarded people. *Psychopharmacology Bulletin, 25,* 358-363.

Gunnell, D., Miller, L.L., Rogers, I., Holly, J.M. & ALSPAC Study Team (2005) Association of insulin-like growth factor I and insulin-like growth factor-binding protein-3 with intelligence quotient among 8- to 9-year-old children in the Avon Longitudinal Study of Parents and Children. *Paediatrics,* 116(5), 6818-6.

Haddad, N.G., Eugster, E.A. (2005). Hypopituitarism and neurodevelopmental abnormalities in relation to central nervous system structural defects in children with optic nerve hypoplasia. *Journal of Paediatric Endocrinology and Metabolism,* 18(9), 853-858.

Hadley, M. E. (2000). *Endocrinology.* Prentice Hall: Upper Saddle River, New Jersey.

Hammill, D. D., Crandell, J. M., Jr., & Colarusso, R. (1970). The Slosson Intelligence Test adapted for visually limited children. Exceptional Children, 36 (7), 535-536.

Happé, F. G. E. (1994a). Annotation: Psychological theories of autism. *Journal of Child Psychology and Psychiatry*, 35, 215–229.

Hardan, A. Y., Minshew, N. J., & Keshavan, M. S. (2000). Corpus callosum size in autism. *Neurology*, 55, 1033-1036.

Harris, P. L. (1991). The Work of the Imagination. In A. Whiten. *Natural Theories of Mind.* Oxford : Blackwell.

Harrison, I.A., Brosnahan, D., Phelan, E.,. Fitzgerald, R.J., Reardon, W. (2004). Septo-optic dysplasia with digital anomalies - a recurrent pattern syndrome. *American journal of medical genetics* A, 131(1), 82 – 85.

Harrison, P.L., & Oakland, T. (2003), *Adaptive Behavior Assessment System – Second Edition,* San Antonio, TX: The Psychological Corporation.

Hashimoto, T., Tayama, M., Murakawa, K., Yoshimoto, T., Miyazaki, M., Harada, M., & Kuroda, Y. (1995)/ Development of the brainstem and cerebellum in autistic patients. *Journal of. Autism and Developmental Disorders*, 1, 1–18.

Herzig, M.E., Snow, M.E., & Sherman, M. (1989). Affect and Cognition in Autism, *Journal of the American Academy of Child and Adolescent Psychiatry*, 28, 195-199.

Hobson, P. (2005). Why connect? On the relation between autism and blindness. In L. Pring (Ed.) *Autism and Blindness: Current Research and Reflections.* Whurr London/Philadelphia.

Hobson, R.P., & Bishop, M. (2003). The pathogenesis of autism: Insights from congenital blindness. *Philosophical Transactions of the Royal Society of London Series B–Biological Sciences*, 358, 335–344.

Hobson, R. P., Brown, R., Minter, M. E., & Lee, A. (1997). "Autism" revisited: The case of congenital blindness. In V. Lewis & G. M. Collis (Eds.), *Blindness and psychological development in young children* (pp. 99-115). Leicester, England: British Psychological Society Books.

Hobson, R.P. (1993). *Autism and the development of mind.* Hillsdale, NJ: Lawrence Erlbaum Associates.

Hobson, R.P., Lee, A. & Brown, R. (1999). Autism and congenital blindness. *Journal of Autism and Developmental Disorders*, 29(1), 45-56.

Holladay, J. (1997). Proper method for calculating average visual acuity. *Journal of Refractory Surgery*, 13 (4), 388 –391.

Hollander, E., DelGiudice-Asch, G., Simon, L., Schmeidler, J., Cartwright, C., DeCaria, C.M., Kwon, J., Cunningham-Rundles, C., Chapman, F., & Zabriskie, J.B. (1999). B lymphocyte antigen D8/17 and repetitive behaviors in autism. *American Journal of Psychiatry*, 156(2), 317-320.

Hollander, E. Novotny, S., Allen A., Aronowitz., Cartwright, C., & Decaria, C. (2000). The relationship between repetitive behaviors and growth hormone response to sumatriptan challenge in adult autistic disorder. *Neuropsychopharmacology*, 22 (2), 163-167.

Hoshino, Y., Kaneko M., Yashima, Y., Kumashiro, H., Volkmar F.R., & Cohen, D.J. (1987). Clinical Features of Autistic Children with Setback Course in Their Infancy *The Japanese Journal of Psychiatry and Neurology*, 41, (2), 237-245.

Howlin, P., & Karpf, J. (2004) Using the Social Communication Questionnaire to identify autistic spectrum disorders associated with other genetic conditions- findings from a study of individuals with Cohen Syndrome, *Autism*, 8, 175-182.

Howlin, P., & Moore, A. (1997) Diagnosis in autism - a survey of 1200 patients, *Autism,* 1(2), 135-162.

Howlin, P.(2003). *Preparing for adulthood,* (2nd edition), London: Routledge

Howlin, P (2000) Outcome in adult life for more able individuals with autism or Asperger syndrome, *Autism, 4, 1,* 63-83

Hoyt, C.S., & Billson, F.A. (1978): Maternal anticonvulsants and optic nerve hypoplasia. *British Journal of Ophthalmol*ogy, 62, 3–6.

Hoyt, C.S., & Billson, F.A. (1986) Optic nerve hypoplasia: changing perspectives. *Australian and New Zealand Journal of Ophthalmology,* 14 (4), 325 –331.

Hoyt, W.F., Kaplan, S.L., Grumbach, M.M., & Glaser, J.S. (1970). Septo-optic dysplasia and pituitary dwarfism. *Lancet,* 1 (7652),_893 –894.

Hultman, C.M. (2002) Perinatal risk factors for infantile autism. *Epidemiology,* 13, 417-423.

Hughes, M., Dote-Kwan, H., & Dolendo, J.(1999). Characteristics of maternal directiveness and responsiveness with young children with visual impairments, *Child: Care, Health and Development* 25,285–298.

Hume, R.F. Jr, Gingras, J.L., Martin, L.S., Hertzberg, B.S., O'Donnell, K., & Killam, A.P. (1994). Ultrasound diagnosis of fetal anomalies associated with in utero cocaine exposure: further support for cocaine-induced vascular disruption teratogenesis. *Fetal Diagnosis therapy,* 9:239–245.

Hynd, G.W., Hall, J., Novey, E.D., Eliopulos, D., Black, K., Gonzalez, J.J., Edmonds, J.E., Riccio, C., & Cohen, M. (1995). Dyslexia and Corpus Callosum Morphology. *Archives of Neurology,* 52(1), 32-38.

Ingudomnukul, E., Baron-Cohen, S., Wheelwright, S., Knickmeyer, R. (2007). Elevated rates of testosterone-related disorders in women with autism spectrum disorders. *Hormones and Behavior,* 51 (5), 597-604.

Insel, T.R., & Young, L.J. (2001). Neurobiology of social attachment. *Nature Neuroscience. Review,* 2,129–136.

Insel, T.R., O'Brien, D.J., & Leckman, J.F (1999). Oxytocin, vasopressin, and autism: is there a connection? *Biological Psychiatry,* 45(2), 145 – 157.

International Molecular Genetic Study of Autism Consortium. (1998). A full genome screen for autism with evidence for linkage to a region on chromosome 7q. *Human Molecular Genetics,* 7, 571-578.

Iverson, J. M. & Goldin-Meadow, S (1998). (eds.). The nature and functions of gesture in children's communications, in the New Directions for Child Development series, No. 79, San Francisco: Jossey-Bass.

Jacobson, J. W. (1982). Problem behavior and psychiatric impairment within a Developmentally Disabled Population: I. Behavior Frequency. *Applied Research in Mental Retardation, 3,* 121–139.

Jan, J.E., Freeman, R.D. & Espezel, H. (1994). Eye-poking. *Developmental Medicine and Child Neurology,* 36, 321–325.

Jan, J.E., Freeman, R.D., McCornick, A.Q. Scott, E.P. Robertson, W.D., & Newman, D.E. (1983). Eye-pressing by visually impaired children. *Developmental Medicine and Child Neurology,* 25, 755–762.

Jan, J.E., Robinson, G.C., Kinnis, C., & MacLeod, P.J.M. (1977). Blindness due to optic-nerve atrophy and hypoplasia in children: an epidemiological study. *Developmental Medicine and Child Neurology,* 19 (3), 353 –363.

Janicki, M.P., & Dalton, A.J. (1998). Sensory impairments among older adults with intellectual disability, *Journal of Intellectual and Developmental Disability,* 23, 3–11.

Jolliffe, T., Lansdown, R., & Robinson, C. (1992). Autism: a personal account. *Communication*, 26, 12–19.

Jones, E.A., & Carr, E.G. (2004). Joint Attention in Children with Autism: Theory and Intervention. *Focus on Autism and Other Developmental Disabilities.* 19(1), 13-26.

Jordan, R. & Libby, S. (1997). Developing and using play in the curriculum. In S. Powell and R. Jordan (eds) *Autism and Learning: a guide to good practice.* London: David Fulton Publishers

Jordan, R.R. (1996) Educational implications of autism and visual impairment in Lindfoot, G, Shattock, P, Finnigan, R and Savery, D (Eds) *Psychological Perspectives in Autism Proceedings of Durham Conference,* 5-7 April 1995.

Just, M.A., Cherkassky, V.L., Keller T.A., & Minshew, N.J. (2004). activation and synchronization during sentence comprehension in high-functioning autism: evidence of underconnectivity, *Brain* 127 (8), 1811–1821.

Kabot, S., Masi, W., & Segal, M. (2003). Advances in the diagnoses and treatment of autism spectrum disorders. *Professional Psychology: Research and Practice*, 34, 26-33.

Kanner, L. (1943). Autistic disturbances of affective contact. *Nervous Child,* 2, 217–250.

Howlin P, Karpf J, Turk J. (2004) Behavioural characteristics and autistic features in individuals with Cohen Syndrome. *European Child and adolescent Psychiatry*, 1(3), 4-13.

Kasper, D.L., & Harrison, T.R. (2005). *Harrison's Principles of Internal Medicine.* (16th ed). New York, NY: McGraw-Hill.

Kaufman, F. R., Kaufman, N., Borchert, M., Inlender, T. (n.d) Optic nerve hypoplasia a guide for parents. Retrieved June 05 2007, from http://www.onesmallvoicefoundation.org/images/ONH%20pamphlet_sm.pdf

Keeler, W. (1958). Autistic patterns and defective communication in blind children with retrolental fibroplasia. In Eds in Hoch, P. M., Zubin J. *Psychopathology of Communication.* New York: Grune & Stratton.

Kiernan, C., & Kiernan, D., 1994. Challenging behaviour in schools for pupils with severe learning difficulties. *Mental Handicap Research* 7, 117–201.

Kenworthy L., Charnas L (1995): Evidence for a discrete behavioural phenotype in the oculocerebrolrenal syndrome of Lowe. *American Journal of Medical Genetics,* 59, 283-290.

Kern, J. K., Garver, C. R., Carmody, T., Andrews, A. A., Trivedi, M. H., and Mehta, J. A. (2007). Examining sensory quadrants in autism. *Research in Autism Spectrum Disorders,* 1, 185–193.

Kikuchi, K., Fujisawa, I., Momoi, T., Yamanaka, C., Kaji, M., Nakano, Y., Konishi, J., Mikawa, H., & Sudo, M. (1988). Hypothalamic-pituitary function in growth hormone-deficient patients with pituitary stalk transection. *Journal of Clinical Endocrinology Metabolism*, 67(4), 817-823.

Kim, R.Y., Hoyt, W.F., Lessell, S., & Narahara, M.H.(1989). Superior segmental optic hypoplasia. *Archives of Ophthalmology*, 107, 1312.

Kirk, J., & Butler, G. British Society for Paediatric Endocrinology and Diabetes (BSPED). (2006). *Treatment of Children with Recombinant Human Growth Hormone (r-hG): Shared Care Guidelines. Retrieved* 20th, June, 2007 from http://www.bsped.org.uk/professional/guidelines/docs/SharedcareGH-BSPED.pdf.

Klassen, R. M., Neufeld, P., & Munro, F. (2005). When IQ is irrelevant to the definition of learning disabilities. *School Psychology International, 26*(3), 297-316.

Klein-Tasman, B. P., Mervis, C. B., Lord, C., & Phillips, K. D. (2007). Socio-communicative deficits in young children with Williams syndrome: Performance on the Autism Diagnostic Observation Schedule. *Child Neuropsychology, 13*, 444-467.

Koomar, J. A. & Bundy, A. C. (2002). Creating direct intervention from theory. In A .C. Bundy, S. L. Lane, & E. A. Murray (Eds.) *Sensory integration: Theory and practice* (2nd ed.). Philadelphia: F.A. Davis.

Kraijer, D. W. (1997) *Autism and Autistic-like Conditions in Mental Retardation.* Lisse: Swets & Zeitlinger.

Kraijer, D. (2000). Review of adaptive behavior studies in mentally retarded persons with autism/pervasive developmental disorder. *Journal of Autism and Developmental Disorders*, 30, 39–47.

Kranzler, J.H., Rosenbloom, A.L., Martinez, V., & Guevara-Aguirre, J. (1998) Normal intelligence with severe insulin-like growth factor I deficiency due to growth hormone receptor deficiency: a controlled study in a genetically homogeneous population. *Journal of Clinical Endocrinology and Metabolism*, 83, 1953–1958.

Kravitz, H., & Boehm, J. J. (1971). Rhythmic habit patterns in infancy: Their sequence, age of onset, and frequency. *Child Development*, 42, 399-413.

Krug, D. A., Arick, J. R., & Almond, P. J. (1978). *ABC - Autism Behaviour Checklist.* Portland, OR: ASIEP Education Co.

Kuban, K.C.K., Teele, R.L., & Wallman, J. (1989). Septo-optic-dysplasia-schizencephaly: radiographic and clinical features. *Paediatric Radiology,* 19, 145–150

Kuhn, M.J., Swenson, L.C., & Youssef, H.T. (1993). Absence of the septum pellucidum and associated disorders. *Computerized Medical Imaging and Graphics,* 17(2),137-147

Kytila, J., & Mierrinen, P. (1961). On bilateral aplasia of the optic nerve. *Acta Ophthalmologica Copenh*, 39, 416-419.

La Malfa, G., Lassi, S., Bertelli, M., Salvini, R., Placidi, G.F. (2004). Autism and intellectual disability: a study of prevalence on a sample of the Italian population. *Journal of Intellectual Disability Research*, 48(3), 262-267

Lacey, K.A., & Parkin, J.M. (1974). Causes of short stature: A community study of children in Newcastle Upon Tyne. Lancet, 1, 42–45.

Lamb, J.A., Barnby, G., Bonora, E., Sykes, N., Bacchelli, E., Blasi, F., Maestrini, E., Broxholme, J., Tzenova, J., Weeks, D., Bailey, A.J., & Monaco, A.P. (2005). Analysis of IMGSAC autism susceptibility loci: evidence for sex limited and parent of origin specific effects. *Journal of Medical Genetics*, 42(2), 132-7.

Lambert, S.R., Hoyt, C.S., & Narahara, M.H. (1987). Optic nerve hypoplasia. Survey *of ophthalmology*, 32(11), 1-9.

Lau, K. Y., W. Tam, P. K. Lam and B. P. Wood 1993 Radiological cases of the month. Septo-optic dysplasia (De Morsier syndrome). *American Journal of Diseases in Childhood,* 147, 71-72

Law, C.M. (1987). The disability of short stature. *Archives of Diseases in Childhood,* 62(8), 855-859.

Lavis, D. (1994). One step ahead: aspects of sensory impairment and the ageing process. *RNIB Focus, 13.*

Lecavalier, L. (2005). An evaluation of the Gilliam Autism Rating Scale. *Journal of Autism and Developmental Disorders*, 35, 795-805.

Leekam, S. R., Libby, S., Wing, L., Gould, J. & Taylor, C. (2002). The Diagnostic Interview for Social and Communication Disorders: Algorithms for ICD-10 Childhood Autism and Wing & Gould Autistic Spectrum Disorder. *Journal of Child Psychology and Psychiatry*, 43(3), 327-342.

Leekam, S.R., Nieto, C., Libby, S.J., Wing, L., & Gould, J. (2006). Describing the sensory abnormalities of children and adults with autism. *Journal of Autism and Developmental Disorders,* 37(5), 894-910.

Leloup, E., & Delbeke, P. (2007). Septo-optic dysplasia (de Morsier syndrome). *Bulletin de la Société belge d'ophtalmologie*, 305, 45-48.

Leonard, H.L., Goldberger, E.L., Rapoport, J.L., Cheslow, D.L., Swedo, S.E. (1990). Childhood rituals: normal development or obsessive-compulsive symptoms? *Journal of American Academic Child Adolescent Psychiatry,* 9(1)17-23.

Leonhardt, E.E., & Phil-Ann, T.S (2005). Septo-Optic Dysplasia: A Neurosonographic Review. *Journal of Diagnostic Medical Sonography*, 21, (6), 479-486.

Lewis, V., Norgate, S., Collis, G., & Reynolds, R. (2000). The consequences of visual impairment for children's symbolic and functional play. *British Journal of Developmental Psychology, 18,* 449-464

Libby, S., Powell, S., Messer, D., & Jordan, R. (1998). Spontaneous play in children with autism: a reappraisal. *Journal of Autism and Developmental Disorders,* 28 (6), 487-497.

Lockyer, L., & Rutter, M. (1969) A five- to fifteen-year follow-up study of infantile psychosis. *British Journal of Psychiatry*, 115, 865–882.

Lönn, L., Kvist, H., Grangård, U., Bengtsson , B.A, & Sjöström, L. (1993). CT-determined body composition changes with recombinant human growth hormone treatment to adults with growth hormone deficiency. *Basic Life Sciences*, 60, 229-31.

Lord C, & Volkmar, F. (2002). Genetics of childhood disorders: XLII. Autism, part 1: Diagnosis and assessment in autistic spectrum disorders. *Journal of American Academy and Child Adolescent Psychiatry.* 41(9), 1134-1136

Lord, C., & Risi, S. (1998) Frameworks and methods in diagnosing autism spectrum disorders. *Mental Retardation and Developmental Disabilities Research Reviews,* 4, 90–96.

Lord, C., & Schopler, E. (1987). Neurobiological implications of sex differences in autism. In: Schopler, E. & Mesibov, G.M. (Eds.), *Neurobiological issues in autism.* New York: Plenum Press, pp. 191-211.

Lord, C., Risi, S., Lambrecht, L., Cook, E.H., Leventahal, B.L. & DiLavore, P.C. (2000). The Autism Diagnostic Observation Schedule-Generic: A standard measure of social andcommunication deficits associated with the spectrum of autism. *Journal of Autism and Developmental Disorders,* 30, 205-23.

Lord, C., Rutter, M. & LeCouteur, A. (1994). Autism diagnostic interview-revised: A revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. *Journal of Autism and Developmental Disorders*, 24, 659-85.

Lord, C., Shulman, C., & Di Lavore., P. (2004). Regression and word loss in autistic spectrum disorders. *Journal Child Psychology and Psychiatry*, 45, 936–955.

Lovaas, O., Newsom, C., & Hickman, C., (1987). Self-stimulatory behavior and perception of reinforcement. *Journal of Applied Behavioral Analysis, 20,* 45-68.

Lovaas, O.I, & Simmons, J.Q. (1969). Manipulative of self-destruction in three retarded children. Journal of Applied Behavior Analysis, 2, 143-157.

Loveland K. & Tunali-Kotoski B. (1998) Development of adaptive behavior in persons with mental retardation. In: *Handbook of Mental Retardation and Development* J. A. Burack, R. M. Hodapp & E. Zigler), pp. 521–41. Cambridge University Press, Cambridge, UK.

Loveland, K., Tunali-Kotoski, B., Chen, R., Ortegon, J., Pearson, D.A., Brelsford, K., & Gibbs, M.C. (1997). Affect recognition in autism: Verbal and non-verbal information. *Development and Psychopathology*, 9, 579-593.

Lowenfeld, B. (1981b). Effects of blindness on the cognitive functioning of children. In *Berthold Lowenfeld on blindness and blind people: Selected papers*. New York: American Federation for the Blind.

Lubinsky, M. (1997). Hypothesis: septo-optic dysplasia is a vascular disruption sequence. *American Journal of Medical Genetics,* 69,235–236.

McHugh, E., & Lieberman, L. J. (2003). The impact of developmental factors on stereotypic rocking among children with visual impairments. *Journal of Visual Impairment and Blindness,* 97(8), 453-474.

Maclean-Wood, S.J. (2003). Challenging Behaviour. Understanding and Prevention. *Good Autism Practice*. 4(2), 21-26.

Maestro, S., Casella, C., Milone, A., Muratori, F., & Palacio-Espasa, F. (1999) Study of the onset of autism through home movies. *Psychopathology*, 32, 292-300.

Maghnie, M., Larizza, D., Triulzi, F., Sampaolo, P., Scotti, G., & Severi, F. (1991). Hypopituitarism and stalk agenesis: a congenital syndrome worsened by breech delivery? *Hormone Research*, 35(3-4), 104-108.

Maisto, C. R., Baumeister, A. A., & Maisto, A. A. (1978). An analysis of variables related to self-injurious behavior among institutionalized retarded persons. *Journal of Mental Deficiency Research, 22,* 27-36.

Margalith, D., Jan, J.E., McCormich, A.Q., Tze, W.J., & Lapoint, (1984). Clinical spectrum of congenital optic nerve hypoplasia: review of 51 patients. *Journal of developmental Medicine and Child Neurology,* 26 (3), 311 –322.

Mars, A. E., Mauk, J. E. and Dowrick, P. W. (1998) Symptoms of pervasive developmental disorders as observed in prediagnostic home videos of infants and toddlers. *Journal of Paediatrics*, 132, 500-504.

Mason, G. J. (1991). Stereotypies: A critical review. *Animal Behaviour*, *41*, 1015–1037.

Masel, B.E. (2004). Rehabilitation and Hypopituitarism after traumatic brain injury. *Growth Hormone and IGF Research*, **14** (A), 108–113.

Mazefsky, C. A., & Oswald, D. P. (2006). The discriminative ability and diagnostic utility of the ADOS-G, ADI-R, and the GARS for children in a clinical setting. *Autism, 10*(6), 533-549.

Mazefsky, C.A., & Oswald, D.P. (2006). The discriminative ability and diagnostic utility of the ADOS-G, ADI-R, and GARS for children in a clinical setting, *Autism,* 10,533–549.

Maclean-Wood, A. (2003). Challenging behaviour: Understanding and Prevention. *Good Autism Practice, 4,(2),* 21-26.

Maimburg, R.D., Vaeth, M. (2002) Perinatal risk factors and infantile autism. *Acta psychiatrica scandinavica,* 114, 257-264.

McHugh, E., & Lieberman, L. (2003). The impact of developmental factors on stereotypic rocking in children with visual impairments. Journal of Visual Impairment & Blindness, 97, 453-474.

McKinna, A.J. (1966). Quinine induced hypoplasia of the optic nerve. *Canadian Journal of Ophthalmology,* 1(4), 261–266.
McMahon, C L., & Braddock, S R. (2001). Septo-optic dysplasia as a manifestation of valproic acid embryopathy, *Teratology.* 64(2), 83-6.

McNay, D.E., Turton, J.P., Kelberman, D., Woods, K.S., Brauner, R., Papadimitriou, A., Keller, E. Keller, A., Haufs, N., Krude, H., Shale, S.M., & Dattani, M.T. (2007). *HESX1* mutations are an uncommon cause of septooptic dysplasia and hypopituitarism. *Journal of Clinical Endocrinology and Metabolism,* 92, 691–697.

Mehta, A., & Dattani, M.T. (2008). Developmental disorders of the hypothalamus and pituitary gland associated with congenital hypopituitarism. *Best Practice Research in Clinical Endocrinology and Metabolism,* 22(1), 191-206.

Michaud, J., Mizrahi, E.M., & Urich, H. (1982). Agenesis of the vermis with fusion of the cerebellar hemispheres, septo-optic dysplasia and associated anomalies. Report of a case. *Acta Neuropathologica,* 56(3),161–166

Militerni, R., Bravaccio, C., Falco C., Fico, C., & Palermo, M.T. (2002). Repetitive behaviors in autistic disorder. *European Child & Adolescent Psychiatry,* 11(5), 210 -218.

Millar, S., Chillingworth, A., Bell, A., & Carson, D., McKee, S. (2008). Septo-optic dysplasia with a transverse limb defect. *Clinical Dysmorphology,* 17(2):155-156

Miller, L.J., McIntosh, D.N., McGrath, J., Shyu, V., Lampe, M., Taylor, A.K., Tassone, F., Neitzel, K., Stackhouse, T., & Hagerman, R. (1999) Electrodermal responses to sensory stimuli in individuals with fragile X syndrome: a preliminary report. *American Journal of Medical Genetics,* 83: 268–79.

Miller, S. P., Shevell, M. I., Patenaude, Y., Poulin, C &. O'Gorman, A. M. (2000). Septo-optic dysplasia plus: A spectrum of malformations of cortical development *Neurology* 54, 1701-1703.

Miller, L. J., Lane, S. J., Cermak, S. A., Anzalone, M., & Osten, B. (2005). Regulatory-sensory processing disorders in children. In S. I. Greenspan & S. Wieder (Eds.), Diagnostic manual for infancy and early childhood: Mental health, developmental, regulatory-sensory processing and language disorders and learning challenges (1CDL-DMIC) (pp. 73-112). Bethesda, MD: Interdisciplinary Council on Developmental and Learning Disorders.

Mody, S., Brown, M.R., & Parks, J.S. (2002). The spectrum of Hypopituitarism caused by PROP1 mutations. *Best Practice & Research Clinical Endocrinology & Metabolism,* 16(3), 421 – 431.

Moore, V. & McConachie, H. (1994) 'Communication between blind and severely visually impaired children and their parents. *British Journal of Developmental Psychology,* 12, 491-502.

Mosier, M.A., Lieberman, M.F., Green, W.R., & Knox, D.L. (1978). Hypoplasia of the optic nerve. *Archives of Ophthalmology,* 96(8), 437–1442.

Moss, J., Oliver, C., Hall, S., Arron, K., Sloneem, J., & J. Petty (2005). The association between environmental events and self-injurious behaviour in Cornelia de Lange syndrome. *Journal of Intellectual Disability Research* ,49(4), 269 – 277.

Mukaddes, N.M., Kilincaslan, A., Kucucyazici, G., Sevketoglu, T., & Truncer, S. (2007). Autism in visually impaired individuals. *Psychiatry and Clinical Neurosciences, 61, 39-44*

Mundy, P., Sigman, M., Ungerer, J., & Sherman, T. (1986). Defining the social deficits of autism: The contribution of nonverbal communication measures. *Journal of Child Psychology and Psychiatry,* 27, 657-669.

Murray, P.G., Paterson, W.F., Donaldson, M.D. (2005). Maternal age in patients with septo-optic dysplasia. *Journal of Pediatric Endocrinology and Metabolism*, 18(5), 471-476.

National Organization for Rare Disorders (NORD) (n.d) retrieved December, 12, 2006 from from http://www.rarediseases.org/search/rdbdetail_abstract.html?disname=Septooptic%20Dysplasia

Netchine, I., Sobrier, M.L., Krude, H., Schnabel, D., Maghnie, M., Marcos, E., Duriez, B., Cacheux, V., Moers, A., Goossens, M., Gruters, A., & Amselem, S. (2000). Mutations in LHX3 result in a new syndrome revealed by combined pituitary hormone deficiency. *Nature Genetics*, 25, 182–186.

Newborg J, Stock J., & Wnek L. (1988). *The Battelle Developmental Inventory.* Allen, TX: DLM Teaching Resources.

Newschaffer, C.J., Croen, L.A,, Daniels, J., *et al.* (2007). The epidemiology of autism spectrum disorders. *Annual Review of Public Health*, 28, 235–58.

Newschaffer, C.J., Fallin, D., Lee, N.L. (2002) Heritable and nonheritable risk factors for autism spectrum disorders. *Epidemiologic reviews,* 24, 137-153.

Norris, M., Spaulding, P. J., Brodie, F. H. (1957) *Blindness in Children.* Chicago : The University Press.

Nylander, L., & Gillberg, C. (2001). Screening for autism spectrum disorders in adult psychiatric outpatients: A preliminary report. *Acta Psychiatrica Scandinavica*, 103, 428–434.

Obuchowski, N. A. (2006) An ROC-type measure of diagnostic accuracy when the gold standard is continuous-scale. *Statistics in Medicine*, 25, 481-493.

O'Gorman, G. (1967). *The nature of childhood autism.* London: Butterworths

Ockelford, A., Pring, L., Welch, G., & Treffert, D. (2005). *Focus on Music: Exploring the Musical Interests and Abilities of Blind and Partially-Sighted Children and Young People with Septo-Optic Dysplasia.* London: London Institute of Education Publication
O'Gorman, G. (1967). *The Nature of Childhood Autism.* Butterworths, London.

Oliver, C. (1995) Self-injurious behaviour in children with learning disabilities. *Journal of ChildPsychology and Psychiatry, 30*, 909-92.

Olsson, I., Steffenburg, S., & Gillberg, C. (1988). Epilepsy in autism and autistic like conditions. A population-based study. *Archives of Neurology*, 45(6):666-668.

Olymbios, P. (1999). Language Development of Blind Children. NSW: Royal Blind Society of NSW.

Ornstein, R. E. (1975). *Psychology of Consciousness*. New York: Penguin Books.

Ornitz, E. M.: Neurophysiologic studies of infantile autism. In D. J. Cohen and A. M. Donnellan (Eds.): *Handbook of Autism and Pervasive Developmental Disorders*. John Wiley & Sons, Inc., New York, 1987, pp. 148-165.

Orrico, A., Galli, L., Zapella, M., Monti, L., Vatti GP, Venturi C, Hayek G. (2002). Septo-optic dysplasia with digital anomalies associated with maternal multidrug abuse during pregnancy. *European Journal of Neurology,* 9, 679-682

Orsmond, G.I., Krauss, M.W., & Seltzer, M.M. (2004) Peer relationships and social and recreational activities among adolescents and adults with autism. *Journal of Autism and Developmental Disorders*, 34, 245-56.

Osterling, J., & Dawson, G. (1994). Early recognition of children with autism: a study of first birthday home videotapes. *Journal of Autism and Developmental Disorders*, 24, 247–57.

Ouvrier, R.A., Lewis, D., Procopis, P.G., Billson, F.A., Silink, M., de Silva, M. (1981). Bilateral optic nerve hypoplasia. *Clinical Experimental Neurology*, 18, 52-56.

Ozonoff, S., Pennington, B.F., & Rogers, S.J. (1991a). Executive function deficits in high-functioning autistic individuals: Relationship to theory of mind. *Journal of Child Psychology and Psychiatry and Allied Disciplines, 32*, 1081-1105.

Ozonoff, S., Williams, B. J., Gale, S., & Miller, J. N. (1999). Autism. and autistic behavior in Joubert syndrome. *Journal of Child. Neurology*, 14, 636–641.

Patel, L., McNally, R.J., Harrison, E., Lloyd, I.C., & Clayton, .PE. (2006). Geographical distribution of optic nerve hypoplasia and septo-optic dysplasia in Northwest England. *Journal of Pediatrics*, 148(1), 85-88.

Parr, J., Shaffer, L., Salt, A., & Dale, N. (2008). Autism-related behaviours in young children with Optic Nerve Hypoplasia and Septo Optic Dysplasia. *Archives of Disease in Childhood disability*, 93 (1), A5

Pearce, JM. (2008). Some observations on the septum pellucidum. *European Neurology*, 59(6), 332-334.

Pérez-Pereira M., & Conti-Ramsden, G. (1999). *Language development and social interaction in blind children.* Hove, England: Psychology Press Ltd.

Perner, J., & Lang, B. (1999). Development of theory of mind and executive control", *Trends in Cognitive Sciences*, 3, 337-344.

Perner, J., & Wimmer, H. (1985) "John thinks that Mary thinks that..." Attribution of second-order beliefs by 5-10 year old children. *Journal of Experimental Child Psychology*, 39, 437-471.

Peterson, R.A., & Walton, D.S. (1997). Optic nerve hypoplasia with good visual acuity and visual field defects: a study of children of diabetic mothers. *Archives of Ophthalmology*, 95, 254-258.

Peters, S.U., Beaudet, A.L., Madduri, N., & Bacino, C. (2004). Autism in Angelman Syndrome: Implications for Autism Research. *Clinical Genetics*, 66, 530-536.

Perry, A., Condillac, R.A., Freeman, N.L. Dunn Geier J., & Belair, J. (2005). Multi-site study of the Childhood Autism Rating Scale (CARS) in five clinical groups of young children, *Journal of Autism and Developmental Disorders*, 35, 625–634

Philippe, A., Martinez, M., Guilloud-Bataille, M., Gillberg, C., Ratsam, M., Sponheim, E., Coleman, M., Zappella, M., Aschauer, H., van Malldergerme, L., Penet, C., Feingold, J., Brice, A., & Leboyer, M. (1999.) Genome-wide scan for autism susceptibility genes. *Human Molecular Genetics*, 8, 805-812.

Phillips, J.A., & Cogan, J.D. (1994). Genetic basis of endocrine disease: Molecular basis of familial human growth hormone deficiency. *Journal of Clinical Endocrinology and Metabolism*, 78(1), 11-16.

Pilowsky, T., Yirmiya, N., Shulman, C., & Dover, R. (1998). The Autism Diagnostic Interview-Revised and the Childhood Autism Rating Scale: differences between diagnostic systems and comparison between genders. *Journal of Autism and Developmental Disorders*, 28, 143-151.

Pinazo-Durán, M. D., Renau-Piqueras, J., & Guerri, C. (1993). Developmental changes in the optic nerve related to ethanol consumption in pregnant rats. Analysis of the ethanol-exposed optic nerve. *Teratology*, 48, 305–322.

Piven, J., & Folstein, S. (1994). The genetics of autism. In M.L. Bauman & T.L. Kemper (Eds.), *The neurobiology of autism* (pp.18-41). Baltimore: Hopkins Press

Piven, J., Bailey, J., Ranson, B.J., & Arndt, S. (1997). An MRI study of the corpus callosum in autism. *American Journal of Psychiatry*, 154(8), 1051-1056.

Polizzi, A., Pavone, P., Iannetti, P., Gambardella, A., Ruggieri, M. (2005). CNS findings in three cases of septo-optic dysplasia, including one with semilobar holoprosencephaly. *American Journal of Medical Genetics*, 136A (4), 357.

Powell, S.B., Newman, H.A., Pendergast, J.F. & Lewis, M.H. (1999). A rodent model of spontaneous stereotypy: Initial characterization of developmental, environmental, and neurobiological factors. *Physiology and Behavior*, 66, (2), 173-215.

Pratt, C., & Bryant, P. (1990). Young children understand that looking leads to knowing (so long as they are looking into a single barrel). Child Development, 61, 973-983.

Preisler, G. M. (1991). Early patterns of interaction between blind infants and their sighted mothers. *Child: Care, Health and Development*, 17, 65–90.

Preisler, G. M. (1993). A descriptive study of blind children in nurseries with sighted children. *Child: Care, Health and Development, 19*, 295-315

Premack, D. G. & Woodruff, G. (1978). Does the chimpanzee have a theory of mind? *Behavioral and Brain Sciences, 1,* 515-526.

Pring, L. (2005). Building on the sum of the parts. In L. Pring (Eds.) *Autism and Blindness: Research and Reflections*. London/Philadelphia: Whurr publishers.

Pring, L,. & Ockelford, A. (2006) 'Focus on Music: A Survey of Parents of Children with Septo-optic Dysplasia', *British Journal of Visual Impairment and Blindness* 23(2): 58–66.

Prior, M., & Ozonoff, S. (1998). Psychological factors in autism. In Volkmar, F. Ed. *Autism and pervasive developmental disorders, 2nd Ed.* (pp. 1-31). New York, NY: Cambridge University Press.

Prizant, B.M., & Duchan, J.F. (1981). The functions of immediate echolalia in autistic children. *Journal of Speech and Hearing Disorders,* 46(3), 241–249.

Ragusa, L., Elia, M., Scifo, R. (1993). Growth hormone deficit in autism. *Journal of Autism and Developmental Disorders*, 23(2), 421-422.

Rainbow, L.A., Rees, S.A., Shaikh, M.G., Shaw, N.J., Cole, T., Barrett, T.G., & Kirk, J. M. W. (2005). Mutation analysis of POUF-1, PROP-1 and HESX-1 show low frequency of mutationsin children with sporadic forms of combined pituitary hormone deficiency and septo-optic dysplasia. *Clinical Endocrinology,* 62(2), 163-168.

Rapin, I. (1991). Autistic children: diagnosis and clinical features. *Pediatrics,* 87(5, 2), 51-60.

Rang, H.P., Dale, M.M, Ritter, J.M, & Moore, P.K. (2003). Pharmacology. (5th Ed.) Churchill: Livingstone.

Regal, M., Páramo, C., Sierra, S.M., & Garcia-Mayor, R.V. (2001). Prevalence and incidence of Hypopituitarism in an adult Caucasian population in northwestern Spain. *Clinical Endocrinology,* 55 (6), 735–40.

Reidl, S.W., Müllner-Eidenböck, A., Prayer, D., Bernert, G., & Frisch, H. (2002). Auxological, ophthalmological, neurological and MRI findings in 25 Austrian patients with septo-optic dysplasia (SOD). *Hormone Research,* 58 (3),16 –19.

Richler, J., Bishop, S.L., Kleinke, J.R., Lord, C. (2007). Restricted and Repetitive Behaviors in Young Children with Autism Spectrum Disorders. *Journal of Autism and Developmental Disorders*, 37, 73–85.

Riedl, S., Vosahlo, J., Battelino, T., Stirn-Kranjc, B., Brugger, P.C., Prayer, D., Müllner-Eidenböck, A., Kapelari, K., Blümel, P., Waldhör, T., Krasny, J., Lebl, J.,& Frisch, H. (2008), Refining clinical phenotypes in septo-optic dysplasia based on MRI findings. *European Journal of Pediatrics*, 167(11), 269-1276.

Reynell, J (1979) *Manual for the Reynell-Zinkin Scales*. London: National Foundation of Education Research.

Rimland, B. (1964) *Infantile Autism*. Appleton-Century Crofts, New York.

Rimland, B. (1990). Sound sensitivity in autism. *Autism Research Review International*, *4*(1), 6-12.

Risch, N., Spiker, D., Lotspeich, L., Nouri, N., Hinds, D., Hallmayer, J., Kalaydjieva, L., McCague, P., Dimicelli, S., Pitts, T., Nguyen, L., Yang, J., Harper, C., Thorpe, D., Vermeer, S., Young, H., Hebert, J., Lin, A., Ferguson, J., Chiotti, C., Wiese-Slater, S., Rogers, T., Salmon, B., Nicholas, P., Myers, R.M. (1999). A genomic screen of autism: evidence for a multilocus etiology. *American Journal of Human Genet*ics, 65, 493-507.

Ritvo, E.R., & Garber, J.H. (1988). Cerebellar hypoplasia and autism. *The New England Journal of Medicine*, 27, 319(17),1152-1154.

Robin, L. G., Cuccaro, M.L., Hill, D.E., Ivers, B. J., & Goldson, E. (200%). Repetitive behaviors in autism: relationships with associated clinical features. *Research in Developmental Disabilities*, 26, (2), 169-181.

Robins, D.L., Fein, D., Barton, M.L., & Green, J.A. (2005). The Modified Checklist for Autism in Toddlers: An initial study investigating the early detection of autism and pervasive developmental disorders. *Journal of Autism and Developmental Disorders,* 31, 131-144.

Robinson, G.C., & Conry, R.F. (1986). Maternal age and congenital optic nerve hypoplasia: a possible clue to aetiology. *Developmental Medicine and Child Neurol*ogy, 28, 294–298.

Rocha, L., Ackermann, R.F., Engel, J., Tracy, J.I., de Leon. J., Qureshi, G., McCann, E.M., McGrory, A., & Josiassen, R.C. (1996). Repetitive behaviors in schizophrenia: a single disturbance or discrete symptoms? *Schizophrenia Research*, 20, (1), 221-229.

Rodrigue, J.R., Morgan, S.B. & Geffken, G.R. (1991). A comparative evaluation of adaptive behavior in children and adolescents with autism, Down syndrome, and normal development. *Journal of Autism and Developmental Disorders*, 21, 187-196.

Roeyers, H. & van Berckelaer-Onnes, I. A. (1994). Play in autistic children. *Communication and Cognition*, 27 (3), 349-360.

Rogers, M. (1996). Vision impairment in Liverpool: prevalence and morbidity. *Archives of Disease in Childhood,* 74, 299-303.

Rogers, S.J. (2004). Developmental regression in autism spectrum disorders. *Mental Retardation and Developmental Disabilities Research Review* 10 (2), 139–43.

Rogers, S.J., & Di Lalla, D.L. (1990). Age of symptom onset in young children with pervasive developmental disorders. *Journal of American Academic Child Adolescent Psychiatry,* 29, 863-872.

Rogers, S.J., & Ozonoff, S. (2005). "Annotation: what do we know about sensory dysfunction in autism? A critical review of the empirical evidence". *Journal of Child Psychological Psychiatry*, 46, 1255-1268.

Rogers, S.J., Hepburn, S., & Wehner, E. (2003). Parent Reports of Sensory Symptoms in Toddlers with Autism and Those with Other Developmental Disorders. *Journal of Autism and Developmental Disorders*, 33(6), 631-642.

Rogers, S.J., Hepburn, S.L., Stackhouse, T., & Wehner, E. (2003). Imitation performance in toddlers with autism and those with other developmental disorders. *Journal of Child Psychology and Psychiatry,* 44(5), 763-781.

Rogers, S.J., Newhart-Larson, S. (1989). Characteristics of infantile autism in five children with Leber's Congenital Amaurosis. *Developmental Medicine and Child Neurology,* 31(5), 598–608.

Roid, G.H. (2003). *Stanford-Binet Intelligence Scales, Fifth Edition*: Technical manual. Itasca, IL: Riverside Publishing.

Rojahn, J., & Sisson, A. L. (1990). Stereotyped behavior. In: Matson, J. L. (Ed.). *Handbook of Behavior Modification with the Mentally Retarded* (2nd Ed.). New York: Plenum Press

Rona, R.J., Tanner, J.M. (1977). Aetiology of idiopathic growth hormone deficiency in England and Wales. *Archives of Diseases in Childhood.* 52(3), 197-208.

Ruggieri, M., Pavone, P., Polizzi, A., Di Pietro, M., Scuderi, A., Gabriele, A., Spalice, A., & Iannetti, P. (2004). Ophthalmological manifestations in segmental neurofibromatosis type 1. *British Journal of Ophthalmology*, 88(11), 1429-33.

Russell, J. (1997). *Autism as an executive disorder.* Oxford: Oxford University Press.

Rutter, M. (1966a). Behavioural and cognitive characteristics of a series of psychotic children. In J. K. Wing (Ed.) *Early Childhood Autism.* Oxford: Pergamon.

Rutter, M. (1966b) Prognosis: Psychotic children in adolescence and early adult life. In Wing, J. K., *Childhood Autism: Clinical, Educational and Social Aspects* Pergamon Press, London.

Rutter, M. (1999) 'Autism: two-way interplay between research and clinical work', *Journal of Child Psychology and Child Psychiatry*, 40, 169–88.

Rutter, M. (2005). Incidence of autism spectrum disorders: changes over time and their meaning. *Acta Pediatrics*, 94 (1), 2–15.

Rutter, M., Andersen-Wood, L., Beckett, C., Bredenkamp, D., Castle, J,. Groothues, C., Kreppner, J., Keaveney, C., Lord, T., & O'Connor, G. (1999) Quasi-autistic patterns following severe early global privation, *Journal of Child Psychology and Psychiatry*, 40, 537-549.

Rutter, M., Bailey, A., Lord, C., & Berument, S.K. (2003) *Social Communication Questionnaire*. Los Angeles, CA: Western Psychological Services.

Rutter, M., Le Couteur, A., Lord, C. (2003) *Autism Diagnostic Interview-Revised (ADI-R).* Western Psychological Services, Los Angeles.

Sallustro, F., & Atwell, C. W. (1978). Body rocking, head banging, and head rolling in normal children. *Journal of Pediatrics*, 93, 704-708.

Sandler, A., & Wills, D.M. (1985). Preliminary notes on play and mastery in the blind child. *Journal of Child Psychotherapy, 1*, 7–19.

Sandman, C.A., Datta, P.C., Barron, J., Hoehler, F.K., Williams, C., & Swanson, J.M. (1983). Naloxone attenuates self-abusive behavior in developmentally disabled clients. *Applied Research in Mental Retardation, 4,* 5-11.

Sattler, J.M. (1988). *Assessment of children* (3rd ed.). San Diego: Author.

Schatz, J., & Hamdan-Allen, G. J. (1995). Effects of Age and IQ on Adaptive Behavior Domains for Children with Autism. *Journal of Autism and Developmental Disorders,* 25, 51–60.

Schneider, H.J., Aimaretti, G., Kreitschmann-Andermahr, I., Stalla, G.K., & Ghigo, E. (2007). Hypopituitarism. Lancet, 28; 369(9571), 1461-1470.

Schopler, E., Reichler, R.J. & Renner, B.R. (1988). *The Childhood Autism Rating Scale (CARS).* Los Angeles: Western Psychological Services.

Schreibman, L., Heyser, L., & Stahmer, A.C. (1999). Autistic disorder: Characteristics and behavioral treatment. In N. Wieseler & R. H. Hanson (Eds.). *Challenging behavior in people with mental health disorders and severe developmental disabilities* (pp. 39-63). Washington, D.C.: American Association on Mental Retardation.

Shattuck, P.T. (2006). The contribution of diagnostic substitution to the growing administrative prevalence of autism in US special education. *Pediatrics,* 117(4), 1028–1037.

Sheng, H.Z., Zhadanov, A.B., Mosinger, B., Jr, Fujii, T., Bertuzzi, S., Grinberg, A., Lee, E.J., Huang, S.P., Mahon, K.A., & Westphal, H. (1996). Specification of pituitary cell lineages by the LIM homeobox gene Lhx3. *Science*, 272, 1004–1007.

Silverstein, A.B. (1986). Nonstandard standard scores on the Vineland Adaptive Behavior Scales; A cautionary note. *American Journal of Mental Deficiency*, 91, 1-4.

Sizonenko, P.C., Clayton, P.E., Cohen, P., Hintz, R.L., Tanaka, T., & Laron, Z. (2001). Diagnosis and management of growth hormone deficiency in childhood and adolescence. Part 1: diagnosis of growth hormone deficiency. *Growth Hormone and IGF Research*, 11(3), 137-65.

Skellenger, A C., & Hill, E. W. (1994). Effectis of a shared teacher-child play intervention on the play skills of three young children who are blind. *Journal of Visual Impairment and Blindness, 88*, 433–445

Skuse, D. (1987). The psychological consequences of being small. *Journal of Child Psychology and Psychiatry,* 28(5), 641–650.

Skuse, D. H. (2000). Imprinting, the X-chromosome, and the male brain: explaining sex differences in the liability to autism. *Pediatric Research, 47*(1), 9-16.

Skuse, D., Warrington, R., Bishop, D., Chowdhury, U., Lau, J., Mandy, W., & Place, M. (2004). The developmental, dimensional and diagnostic interview (3di): A novel computerized assessment for autism spectrum disorders. *Journal of the American Academy of Child and Adolescent Psychiatry, 43*, 548–558.

Slosson, R.L. (1963). Slosson Intelligence Test for children and adults. Slosson Educational Publications, New York.

Slosson, R. L., Nicholson, C. L., & Hibpshman, T. L. (2002). Slosson Intelligence Test-Revised (3rd ed.). East Aurora, NY: Slosson Educational Publications.

Smits, B. W. & Mommers, M. J. (1976) 'Differences Between Blind and Sighted Children on WISC Verbal Subtests', *New Outlook for the Blind* 70: 240–46.

Sornson, M.W., Wu, W., Dasen, J.S., Flynn, S.E., Norman, D.J., O'Connell, S.M., Gukovsky, I., Carrière, C., Ryan, A.K., Miller, A.P., Zuo, L., Gleiberman, A.S., Andersen, B., Beamer, W.G., & Rosenfeld, M.G. (1996). Pituitary lineage determination by the Prophet of Pit-1 homeodomain factor defective in Ames dwarfism. *Nature*, 28; 384(6607), 327-33.

Soto-Ares, G., Joyes, B., Laemaître, M.P., Vallée, L., Pruvo, J.P. (2003). MRI in children with mental retardation. *Paediatric Radiology,* 33 (5),334 –345.

South, M., Ozonoff, S., & McMahon, W. M. (2007). The relationship between executive functioning, central coherence, and repetitive behaviors in the high-functioning autism spectrum. *Autism, 11,* 441-455.

South, M.,Williams, B. J., McMahon,W. M., Owley, T., Filipek, P. A., Shernoff, E., et al. (2002). Utility of the Gilliam Autism Rating Scale in research and clinical populations. *Journal of Autism and Developmental Disorders,* 32(6), 593-599.

Sparrow, S., Balla, D. & Cicchetti, D. (1984). *Vineland Adaptive Behavior Scales-Interview edition.* Circle Pines, MN: American Guidance Service.

Stanhope, R (2000). Growth hormone treatment of short stature due to intrauterine growth retardation. *Clinical Endocrinology*, 53(6), 665-6.

Stanhope, R., Preece, M.A., & Brook, C.G. (1984). Hypoplastic optic nerves and pituitary dysfunction. A spectrum of anatomical and endocrine abnormalities. *Archives of Disease in Childhood*, 59, 111–114.

Steinhausen, H.C., & Stahnke, N. (1977). Negative impact of growth-hormone deficiency on psychological functioning in dwarfed children and adolescents. *European Journal of Paediatrics*, 126(4),263-70.

Steinkuller, P.G., Du, L., Gilbert, C., Foster, A., Collins, M.L., & Coats, D.K. (1999). Childhood blindness. *Journal of AAPOS: the official publication of the American Association for Pediatric Ophthalmology and Strabismus / American Association for Pediatric Ophthalmology and Strabismus* **3** (1), 26 –**32.**

Stevens, C.A., & Dobyns, W/B. (2004). Septo-optic dysplasia and amniotic bands: Further evidence for a vascular pathogenesis. *American Journal of Medical Genetics,* 125A, 12-16.

Stone, W. L., & Hogan, K. L. (1993) 'A Structured Interview for Identifying Young Children with Autism', *Journal of Autism and Developmental Disorders,* 23,639–52.
Strömland, K, Pinazo-Duran, M.D. (2002) Ophthalmic involvement in the fetal alcohol syndrome: clinical and animal model studies. *Alcohol and alcoholism*, 37, 2-8.

Strömland, K. (1985) Ocular abnormalities in the fetal alcohol syndrome. *Acta Ophthalmologica Scandinavica* 63, (171), 1–50.

Strömland, K. (1987). Ocular involvement in the fetal alcohol syndrome. *Surveys in Ophthalmology,* 31, 277–284.

Strömland, K., & Pinazo-Duran, M.D. (1994): Optic nerve hypoplasia: Comparative effects in children and rats exposed to alcohol during pregnancy. *Teratology,* 50,100–111.

Suh, H., Gage, P.J., Drouin, J., & Camper, S.A. (2003). *Pitx2* is required at multiple stages of pituitary organogenesis: pituitary primordium formation and cell specification. *Development*, 129, 329-337.

Sullivan, A.., Kelso, J., & Stewart, M. (1990). Mothers' views on the ages of onset for four childhood disorders. *Child Psychiatry and Human Development*, 20, 269-278.

Symons, F. (1995). Self-injurious behaviour: a brief review of theories and current treatment perspectives. *Developmental Disabilities Bulletin.*, 23(1), 90-104.

Szatmari P, Bartolucci G, Bremner R. (1989). Asperger's syndrome and autism: comparison of early history and outcome. *Developmental Medicine and Child Neurology,* 31(6):709-20.

Tager-Flusberg, H. (2005). Reflections on the connections between autism and blindness. In L. Pring (Ed.), *Autism and blindness* (pp. 181-1888). UK: Whurr Publishers.

Tajima, T., Hattorri, T., Nakajima, T., Okuhara, K., Sato, K., Abe, S., Nakae, J., & Fujieda, K. (2003). Sporadic heterozygous frameshift mutation of HESX1 causing pituitary and optic nerve hypoplasia and combined pituitary hormone deficiency in a Japanese patient. *Journal of Clinical Endocrinology and Metabolism*, 88(1), 45-50.

Talay-Ongan, A., &. Wood, T. (2000) Unusual sensory sensitivities in autism: a possible crossroads, *International Journal of Disability, Development and Education* **47** (2), 201–212.

Taylor, M., & David' A S. (1997). Agenesis of the corpus callosum: a United Kingdom series of 56 cases. *Journal of Neurology and Neurosurgery Psychiatry*, 64, 131-134

Teal, M.B., Wiebe, M.J. (1986). A validity analysis of selected instruments used to assess autism. *Journal of Autism and Developmental Disorders*, 16, (4), 1573-3432

Teär Fahnehjelm K, Wide K, Flodmark, Ek U, Hellström A. (2003). Posterior ocular malformations in children: somatic, neuroradiological and cognitive aspects. Acta Pædiatrics, 92 (3), 301 –308.

The National Cooperative Growth Study, Stabler, B., Clopper, R.R., Siegel, P.T., Stoppani, C., Compton, P.G., & Underwood, L.E. (1994). Academic achievement and psychological adjustment in short children. *Journal of Development and Behavioural Paediatrics*, 15(1),1-6.

The National Institute of Clinical Excellence (NICE) (2008). Growth failure in (children) - human growth hormone (HGH) (review): final scope retrieved 14, 0ctober 2008 from http://www.nice.org.uk/nicemedia/pdf/HGHFinalProtocol.pdf

Thomas, P.Q., Dattani, M.T., Brickman, J.M., McNay, D., Warne, G., Zacharin, M., Cameron, F., Hurst, J., Woods, K., Dunger, D., Stanhope, R., Forrest, S., Robinson, I.C., & Beddington, R.S. (2001). Heterozygous HESX1 mutations associated with isolated congenital pituitary hypoplasia and septo-optic dysplasia. *Human Molecular Genetics,* 10(1):39–45.

Thomas, P.Q., Johnson, B.V., Rathjen, J., & Rathjen, P.D. (1995). Sequence, genomic organization, and expression of the novel homeobox gene *Hesx1*. *Journal of Biological Chemistry*, 270, 3869–3875.

Tomanik, S., Pearson, D. A., Loveland, K. A., Lane, D. M., & Shaw, J.B. (2007). Increasing the reliability of autism diagnoses: Examining the utility of adaptive functioning. *Journal of Autism and Developmental Disabilities*, *37*, 921-928.

Tonge, B.J. & Einfeld, S.L. (2003). Psychopathology and Intellectual Disability. The Australian Child to Adult Longitudinal Study. In L. Masters Glidden (ed.) International Review of Research in Mental Retardation, Volume 26 (pp 61-91). California: Academic Press

Toogood, A.A., & Stewart, P.M. (2008). Hypopituitarism: clinical features, diagnosis, and management. *Endocrinology and Metabolism Clinics of North America*, 37(1), 235-**61.**

Tornqvist, K., Ericsson, A., & Källén, B. (2002). Optic nerve hypoplasia: Risk factors and epidemiology. *Acta Ophthalmologica Scandinavica,* 80(3), 300-304.

Traggiai, C., & Stanhope, R. (2002). Endocrinopathies associated with midline cerebral and cranial malformations. *Journal of Paediatrics*, 140, 252-5.

Traggiai, C., & Stanhope, R. (2007). Management of growth hormone deficiency in children and adults. *Prescriber*, 18(9), 67-71.

Triulzi, F., Scotti, G., di Natale, B., Pellini, C., Lukezic, M., Scognamiglio, M., Chiumello, & G. (1994). Evidence of a congenital midline brain anomaly in pituitary dwarfs: a magnetic resonance imaging study in 101 patients. *Paediatrics,* 93(3), 409-416.

Troster, H., Brambring, M., & Beelmann, A. (1991a). Prevalence and situational causes of stereotyped behaviors in blind infants and preschoolers. Journal of Abnormal Child Psychology, 19, 569-590.

Troster, H., Brambring, M., & Beelmann, A. (1991b). The age dependence of stereotyped behaviours in blind infants and preschoolers. Child: Care, Health and Development, 17, 137-157.

Tröster, H., & Brambring, M. (1994). The play behaviour and play materials in blind and sighted infants and preschoolers. *Journal of Visual Impairment and Blindness, 88*, 421-432.

Tze, W.J., & Lapointe, J. (1984). Clinical. spectrum of congenital optic nerve hypoplasia: review of 51 patients. *Developmental Medicine and Child Neurology*, 26, 311-322.

UK Child Growth foundation. Growth Hormone Deficiency. Retrieved from 14, October 2005.http://www.childgrowthfoundation.org/pdf_files/Booklets/02_Growth_Hormone_Deficiency.pdf

Urwin, C. (1983) Dialogue and cognitive functioning in the early language development of three blind children. In: *Language Acquisition in the Blind Child: Normal and Deficient*A. E. Mills), pp. 142–161. Croom-Helm, London, UK.

Vance, M.L. (1993). Metabolic status and growth hormone secretion in man. *Journal of Paediatric Endocrinology*, 6(3-4), 267-72.

Van Hasselt, V. B., Kazdin, A. E. & Hersen, M. (1986). Assessment of problem behaviours in visually handicapped adolescents. *Journal of Clinical Child Psychology*, 15, 134-141

Vidal, C., Nicolson, R.,. DeVito, T., Hayashi, K.,. Geaga, J., Drost, D., Williamson, P., Rajakumar, N., Sui, Y., & Dutton, R. (2006). Mapping Corpus Callosum Deficits in Autism: An Index of Aberrant Cortical Connectivity. *Biological Psychiatry*, 60, (3), 218 – 225.

Vieira, T, C., Boldarine, V.T., & Abucham, J. (2007). Molecular analysis of PROP1, PIT1, HESX1, LHX3, and LHX4 shows high frequency of PROP1 mutations in patients with familial forms of combined pituitary hormone deficiency. *Arquivos Brasileiros de Endocrinologia e Metabologia*, 51(7), 1097 103.

Vimpani, G.V., Vimpani, A.F., Lidgard, G.P., Cameron, E.H., & Farquhar, J.W. (1977) Prevalence of severe growth hormone deficiency. *British Medical Journal*, 13(2), 427-30.

Volkmar F. R., Sparrow S. S., Goudreau D., Cicchetti D. V., Paul R. & Cohen D. J. (1987) Social deficits in autism: an operational approach using the Vineland Adaptive Behavior Scales. *Journal of the American Academy of Child and Adolescent Psychiatry* 26, 156–61.

Volkmar, F.R. (1999). The screening and diagnosis of autism spectrum disorders. *Journal of Autism and Developmental Disorders*, 29(2), 439-484.

Volkmar, F.R., Stier, D.M., & Cohen, D.J. (1985). Age of recognition of pervasive developmental disorder. *American Journal of Psychiatry*, 142(12), 1450-1452.

Wagner, J.K., Eble, A., Hindmarsh, P.C., & Mullis, P.E. (1998). Prevalence of human GH-1 gene alterations in patients with isolated growth hormone deficiency. *Paediatric Research*, 43, 105-110.

Wales, J.K., & Quarrell, O.W. (1996). Evidence for possible Mendelian inheritance of septo-optic dysplasia. *Acta Paediatrica*, 85, 391–392.

Walton, D.S. & Robb, R.M. (1970) Optic nerve hypoplasia. A report of 20 cases. *Archives of Ophthalmology,* 84(5), 572–578.

Warburg M. (2001). Visual impairment in adult people with intellectual disability: literature review. *Journal of Intellectual Disability Research*, 45(5), 424–38.

Warren, D. (1984). *Language development, in Blindness and Early Childhood; Second Edition,* New York: American Foundation for the Blind.

Warren, D. H. (1994) *Blindness and Children: An Individual Differences Approach* Cambridge University Press, New York, USA.

Wechsler, D. (1991). *Manual for the Wechsler intelligence scale for children* (3rd ed.). San Antonio, TX: The Psychological Corporation.

Wellman, H., & Estes, D. (1986). Early understanding of mental entities: a re- examination of childhood realism. *Child Development*, 57, 910-923.

Wellman, H.M., & Lagattuta, K. H. (2000). Developing understandings of mind. In S. Baron-Cohen, H. Tager-Flusberg, & D. Cohen (Eds.), *Understanding other minds: Perspectives from developmental cognitive neuroscience, second edition.* Oxford, UK: Oxford University Press.

Werner, E., Dawson, G., Osterling, J. & Dinno, N. (2000) Brief report: Recognition of autism spectrum disorder before one year of age: A retrospective study based on home videotapes. *Journal of Autism and Developmental Disorders*, 30, 157-162.

Whirney, R.D., & Blodi, F.C., (1963). Hypoplasia of the optic nerve – a clinical and histopathologic correlation. *Transactions - American Academy of Ophthalmology and Otolaryngology*, 67, 733–738.

Williams, J., Brodsky, M., Griebel, C., Glasier, M., Caldwell, D., & Thomas, P. (1993). Septo-Optic Dysplasia: The Clinical Insignificance of an Absent Septum Pellucidum. *Developmental Medicine and Child Neurology*, 35, 490-501.

Willnow, S., Kiess, W., Butenandt, O., Dorr, H.G., Enders, A., Strasser-Vogel, B., Egger, J., & Schwarz, H.P.(1996). Endocrine disorders in septo-optic dysplasia (de Morsier syndrome) - evaluation and follow-up of 18 patients. *European Journal of Paediatrics*, 155,179-184.

Wills, D.M. (1968). Problems of play and mastery in the blind child. *British Journal of Medical Psychology,* 41(3), 213–222.

Wimmer, H., & Perner, J. (1983). Beliefs about beliefs: Representation and constraining function of wrong beliefs in young children's understanding of deception. *Cognition,* 13, 103-128.

Wing, L. (1969). The handicaps of autistic children: A comparison study. *Journal of Child Psychology and Child Psychiatry*, 10, 1–40.

Wing, L., & Gould, J. (1979). Severe impairments of social interaction and associated abnormalities in children: epidemiology and classification. *Journal of Autism and Developmental Disorders*, 9, 11-29.

Wing, L., Leekam, S. R., Libby, S. J., Gould, J., & Larcombe, M. (2002). The Diagnostic Interview for Social and Communication Disorders: Background inter-rater reliability and clinical use. *Journal of Child Psychology and Psychiatry*, 43, 307–325.

World Health Organisation. (1967). *International statistical classification of diseases and related health problems, (8th Ed) (ICD 8).* Geneva: World Health Organisation.

World Health Organisation. (1992). *International statistical classification of diseases and related health problems, (10th Ed) (ICD 10).* Geneva: World Health Organisation.

World Health Organisation. (2O00). *International statistical classification of diseases and related health problems, (8th Ed) (ICD 8).* Geneva: World Health Organisation.

Yirmiya, N., & Shaked M. Psychiatric disorders in parents of children with autism: a meta-analysis. *Journal of Child Psychology and Psychiatry*, 46(1), 69-83.

Zeki S.M (1990). Optic nerve hypoplasia and astigmatism: a new association. *British Journal of Ophthalmology,* 74(5). 297-299.

Zeki, S.M., & Dutton, G.N. (1990). Optic nerve hypoplasia in children. *British Journal of Ophthalmology*, 74(5):300-304.

Zhu, X., & Rosenfeld, M.G. (2004). Transcriptional control of precursor proliferation in the early phases of pituitary development. *Current Opinions in Genetic Development*, 14(5), 567-74.

Appendix A

INVITATION TO PARTICIPATE IN A RESEARCH STUDY

I am carrying out research as part of my PhD at the Applied Developmental Psychology Department at the University of Birmingham.

WHAT IS THE PURPOSE OF THE STUDY

My research explores children's understanding that other people have their own plans, thoughts, and points of view using pretend play. Some children have difficulties in understanding that other people's beliefs, attitudes, and emotions about the same situation maybe different to their own.

DOES MY CHILD HAVE TO TAKE PART

Your child does not have to take part, but their participation will be greatly appreciated.
If, for any reason your child appears bored, does not want to talk, or indicates in any other way that he or she does not wish to participate, he/she will be able to return to their regular study at any time. All data will remain anonymous and confidential.

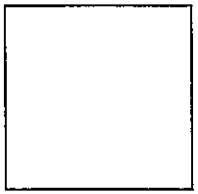
WHAT WILL HAPPEN IF MY CHILD TAKES PART?

I have previously piloted these play tasks in schools and all children commented on the fun nature of the tasks, so hopefully children will go on to enjoy the tasks. Tasks will include pretend play, grouping of familiar words and simple number recalling.
I have enclosed a consent form and two short questionnaires. Please send these back to your child's school in the envelope provided if you decide to take part.
The school will receive a three pound voucher for each child who participates.

Please do not hesitate to contact me as I can send you additional information to you.

Jagjeet Jutley
University of Birmingham
School of Psychology
Bristol Road
Birmingham
B15 2TT
Tel: 01214143507
Email:jkj379@bham.ac.uk

Appendix B



INVITATION TO PARTICIPATE IN A RESEARCH STUDY LOOKING AT HOW CHILDREN DEVELOP THE ABILITY TO UNDERSTAND THE THOUGHTS AND FEELINGS OF OTHERS.

WHAT IS THE PURPOSE OF THE STUDY

My research explores children's understanding that other people have their own plans, thoughts, and points of view using pretend play. Some children have difficulties in understanding that other people's beliefs, attitudes, and emotions about the same situation may be different to their own.

Previous research has highlighted that visually impaired children can show a delay in developing these abilities. My research aims recreate previous research but with the use of objects which are more familiar to visually impaired children.

DOES MY CHILD HAVE TO TAKE PART

Your child does not have to take part, but their participation will be greatly appreciated.

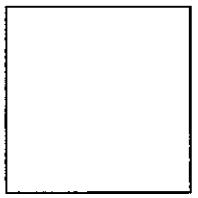
If, for any reason your child appears bored, does not want to talk, or indicates in any other way that he/ she does not wish to participate, he/she will be able to return to their regular activities All data will remain anonymous and confidential.

WHAT WILL HAPPEN IF MY CHILD TAKES PART?

I have previously piloted these play tasks in a school for the visually impaired and all children commented on the fun nature of them. Activities will include a verbal story with props and without, grouping of familiar words and simple number recall backwards and forwards. In total the assessment will last approximately thirty minutes.

If you would like to participate please email me back. Each child will also receive ten pounds in educational vouchers

Please do not hesitate to contact me with any questions or queries or if you would like any additional information



Jagjeet Jutley
University of Birmingham
School of Psychology
Bristol Road
Birmingham
B15 2TT
Tel: 01214143507
Email:jkj379@bham.ac.uk

Demographic Questionnaire

Please return with the consent form.

1) Please indicate for us the medical diagnosis you have for your child

2) Please tell us about your child's vision (tick one box only)

Does she/he have?

No vision ☐

Some light perception but no pattern perception ☐

Some light perception/shape/movement perception ☐

Partial sight ☐

3) Your Child's age _____

4) Gender M/F

5) Ethnicity _____

INVITATION TO PARTICIPATE IN A RESEARCH STUDY LOOKING AT HOW CHILDREN DEVELOP THE ABILITY TO UNDERSTAND THE THOUGHTS AND FEELINGS OF OTHERS

CONSENT FORM

If you allow your child to take part in the study please complete the consent form and return it to the school within two weeks of receiving it this pack.

	Please tick box
I understand that my child's participation is voluntary and that I am free to withdraw my child at any time, without giving any reason.	☐
I agree to allow my child _____ to take part in the research project.	☐

_____ _____ _____

Name of Guardian Date Signature

_____

Name of Child

Appendix C

Modules of ADOS and Adaptations for Visually Impaired Children

Below are the descriptions of the activities and the purpose of each activity for modules one to three. Module four has not been described as this module is intended for older adolescents or adults. Some of the toys and activities have been modified to make allowances for impairments in children's vision. However, these modifications still aim to measure the same behaviours as does the original module but children will use either tactile or auditory senses instead of vision as alternative routes of expression.

Module one

Module one is intended for use with children with an expressive language level of no speech or simple phrases.

The module consists of ten activities with 29 ratings which code language and communication (non-echoed language, frequency of vocalisation directed to others, Intonation of vocalisations or verbalisations and immediate echolalia, stereotyped/idiosyncratic use of words or phrases, use of others body to communicate, pointing and gestures). Reciprocal social interaction which includes; unusual eye contact, which will be amended to unusual body orientation, responsive social smile, facial expression directed to others and integration of gaze and other behaviours during social overtures, shared enjoyment in interaction, response to name, giving, showing, spontaneous initiation of joint attention and response to joint attention and requesting. The module also explores play and specifically functional play with objects and imagination and creativity.

1. Free play.

Purpose: As warm up period to assess the independent use of toys, any presence of repetitive behaviours and engagement with parent/caregiver during free play in a new environment.

Materials and instructions: A pop-up toy (change for auditory toy), board book, toy telephone, four pieces of yarn (change into 4 different textured yarns varying in thickness), textured block, music box, dump truck, baby doll, letter blocks, medium size ball, two identical cars, two pairs of small balls, two small utensils.

Additional materials or substitutions for visually impaired children

- Baby doll – substituted for "Baby Annabel" which babbles, gurgles and giggles (extra auditory sounds). The doll also moves her mouth, burps and cries.
- The toy telephones with replaced with "laugh and learn –learning phone fisher-price, which has a light up display and nine musical songs.
- The two pieces of yarn will be replaced with thicker pieces of string instead.

The parent/caregiver is present and sits a few feet away from the child. They are advised the purpose of the activity is to get the child to adjust to the new environment. The examiner engages the parent in conversation by asking them "what type of toys the child like to play with at home? If the child is comfortable playing independently they are left to do so for three minutes. After three minutes the parent is asked to engage the child in free play. Activities 2, 3 and 6 can also be assessed in this activity.

2. Response to name.

Purpose: assess response to name
Materials and instruction: any toys from free play. The examiner is positioned so that the child can turn ~~look~~ towards them when the child's name is called.

3. Response to joint attention.

Purpose: elicit eye contact coordination with facial orientation, verbalisation, and pointing in order to draw the child's attention to a distant object.
Materials and instructions: Remote controlled bunny or Car

The child's name is called or the child is touched to attract their attention and the examiner says "look" (in case of visually impaired children, "feel") and looks towards the toy/containers (for visually impaired child, guide child to bunny rabbit or turn on rabbit to make noise for child to follow)

The examiner watches to see if the child follows your gaze **or turns to examiner or bunny rabbit, which can be assessed by body orientation.** They toy is activated and turned off. The examiner waits to see if the child requests the toy by reaching, looking, and/or vocalising.

4. Bubble Play.

Purpose: elicit eye contact **or body orientation towards the examiner and vocalisation** from the child with coordination with his/her pointing or reaching in order to direct attention of the parent/caregiver to a distant object.
Materials and instructions: bubble gun and bubble liquid. The opportunity is given to see if the child requests more bubble. The experimenter stops to see if the requests more bubbles or the toy from the examiner.
Substitutions for visually impaired children: **Scented and brightly coloured "gazillion bubbles" which are directed towards child's arm**

5. Anticipation of a routine with objects.

Purpose: assess child's anticipation and initiation of repetition of an action routine with objects.
Materials and instructions: a balloon or cause and effect toy. A large balloon is blown up slowly, and pinched at the neck. The child is encouraged to touch the balloon and alerting them they are ready to let go.
Substitutions for visually impaired children: Jack in the box or pop up toy from free play

6. Responsive social smile.

During any activity or with any toy

7. Anticipation of a social routine.

Purpose: assess the child's anticipation of, request for and participation in social routine.
Materials and instruction: baby blanket for use in peek-a-boo. Peek-a-boo doll with excitement to elicit anticipation.
Substitutions for visually impaired children: child is tickled or blanket is skimmed over child's face

8. Functional and symbolic function.

Purpose: observe child's imitation of simple actions with real objects and with non-meaningful placeholders for the same object.
Materials and instructions: toy car, frog that squeaks, toy cup, toy airplane, toy flower and plain cylindrical block.
The examiner places all the toys on the table and selects the car and moves the car along the table saying "look at the car vroom vroom" the car is given to the child and the child is asked to do the same. If the child imitates then positive feedback is given (claps and cheers). If the child does not imitate the action the child is helped to do so.
Substitutions for visually impaired children: Child hand is placed on the examiner throughout the task.

9. Birthday party.

Purpose: create the opportunity to engage in symbolic and functional play.
Materials and instructions: baby doll, plate, fork, knife, cup, napkin, play-doh, four candles and blanket.

Activity is carried out at a slow pace to allow the opportunity for the child to initiate or join in with activities with the doll. The doll is placed on the table and the child is free to touch and hug the doll. The child is told it's the baby's birthday and they will have a party for her. A cake is made out of the play-dough. The candles are given to the child so they can place them on the cake. The examiner pretends to light the candles and vocalises that they are hot. The examiner asks the child what should do next and then they sing happy "birthday" and blow out the candles. The examiner pretends to cut the cake and eat it and states the baby is hungry (prompt to feed the baby). The child is advised the party is over and the baby need to sleep.

Substitutions for visually impaired children

- **Scented play- dough**
- **Baby Annabel, who vocalises**
- **Larger utensils (knife and fork) and candles.**

10. Snack.

Purpose: opportunity to make request in a familiar context.
Materials and instructions: small cup, juice, plate and small cookies.

Module 2

Module two is intended for children with an expressive language level of flexible three word phrases or verbally fluent. Module two consists of 14 activities and 28 ratings, coding is similar to module one, but stereotyped and repetitive behaviours are coded and the quality and amount of behaviours is also assessed.

1. Construction task.

Purpose: warm up activity, observe child's interactive behaviour and allow for observation of whether the child asks for help.
Instructions and materials: the instructions and materials have been modified as children in the present study have visual impairments and the task relies heavily on visual-spatial information.
Wooden matching set that develops tactile discrimination as the child feels the textured knobs and places them in the correct textured hole.
The child is asked to assemble corresponding textured blocks to construct a design. Some blocks are placed out of reach of the child but still in their view (or told of the extra blocks) which will prompt the child to ask for help in order to complete the task (if not examiner may as "do we need more blocks? or Let me know if you need more blocks?). When task is finished the container for the blocks is placed in front of the child and the child is directed to the opening of the container and advised to put the blocks inside and close the lid.

Materials are purchased from the RNIB website.

Response to name.

Purpose: assess response to name
Instructions and materials: any toys from module two and can take place anytime during the assessment. When the child is playing with a toy and the examiner is positioned so the child can turn around at look at the examiner from a distance of 3 -5 feet the child's name is called.

3. Make - believe play.

Purpose: observe child's creative or imaginative or creative use of miniature play of objects in an unstructured task.
Materials and instructions: Family set of human dolls and a dog with accompanying furniture and props that "match" the dolls: a miniature book: small plates and spoons, a little plate, pieces of miniature food: a toy car, a toy rocket: a small ball: a hologram (need to change) and two pieces of junk (a cloth and piece of jewellery)

The materials are laid out and the child is told "this is a family, with a mother and father, and a young girl/boy and a baby. Here are some other things. Could you play with these for a while?" If child does not the examiner helps and asks questions about what is happening etc...

4. Joint interactive play.

Purpose: assess the degree and quality of the child's coordination of behaviour and affect with the examiner in joint interactive play.

Materials and instructions: materials are from make-believe task. After the child has initiated sufficient make believe play, the examiner asks the child if they can play too. The examiner begins to manipulate the objects to produce a press for joint interactive play. For example the examiners doll may pick up an object and give it to the child's doll.

5. Conversation.

Purpose: assess the child's ability to carry out minimal conservation with back and forth interchange, and generate a language sample in less structured way.
Materials and instructions: examiner can initiate conversation at any time during the schedule.

6. Response to joint attention.

Purpose: assess the child's response to the examiner use of eye contact coordinated with facial orientation, verbalization, and pointing, in order to draw attention to a distant object.
Materials and instructions: remote controlled car, and examiner (will be changed for a toy with auditory sounds.) asks the child, "can you hear the toy" which direction is it in. child should orient to toy. Examiner will be sat next to child and child should co-ordinate between sound of toy and to examiner.
n.b., this task is not scored but is used to gather pressures

7. Demonstration task.

Purpose: ability to communicate about familiar series of actions using gesture or mime with gesture and language.
Materials and instruction: Hand and soap. Examiner asks child to play pretend game. **Examiner places child's hand over theirs and describes scenario**

8. Description of picture scene.

Purpose: generate a sample of language and/other communicative behaviours
Materials and instructions: feast scene or resort scene. The child is asked to look at the scene. The examiner asks "can you tell me about it"

Substitutions for visually impaired children

- Picture will be exchanged for a raised picture. Examiner asks child to **feel**/look at and describe what's happening in the picture?

9. Telling a story from a book.

Purpose: assess child's ability to follow comment on sequential story in a picture book and to generate language.

Materials and instructions: presented with book and told to look at it. Examiner tells child the start of the story and asks the child if they can tell the rest of the story from the pictures. The story book will be exchanged for one for children with visual impairments.

10. Free play.

As module one or toys from make believe task.

11. Birthday party.

As module one

12. Snack.

As module one

13. Anticipation of a routine with object.

As module one

14. Bubble play.

As module one

Module 3 and 4

Module three intended for children with an expressive language level, being a verbally fluent/ child to adolescent. Module three consists of 14 activities and 28 ratings which report more detailed information about conversational skills, empathy, insight, compulsions, rituals and self-injurious behaviour

1. Construction task

Block puzzle as in module two.2. Make believe play

Purpose: to observe the participant's creative or imaginative play in an unstructured task. Materials are chosen specific to the child's interests

Materials: bag three: two male action figures, one female action figure, three "props" (one for each figure") miniature hairbrush, 2 small tools, toy dinosaur.

Bag 2: 2 small spoons, 2 plates and a teapot, pitcher, or measuring cup, toy car, hologram spin disk: and two pieces of junk (cloth and jewellery box)

Instructions: materials are laid out and the child is told here are three characters. The examiner asks the child to play with the toys. Each character is introduced and the child is encouraged to produce a sequence of actions which involve the materials in the task. The tasks primary aim is to assess how the child uses the characters to interact with each other.

Substitutions for visually impaired children

- The child is provided with more descriptions of the characters and materials.

3. Joint Interactive Play

Materials from make believe play and procedure same as module two.

4. Demonstration task.

Purpose: ability to communicate about familiar series of actions using gesture or mime with gesture and language.
Materials and instruction: Hand and soap. Examiner asks child to play pretend game. Examiner places child's hand over theirs and describes scenario

5. Description of a picture

Purpose: provide a sample of language and other communicative behaviours.
Materials and instructions: resort scene. Child is asked to look at picture and asked if they can tell the experimenter about the scene and what is happening.
Substitutions for visually impaired children

- Collage of scene.
- Child is asked if they can tell them more about the beach, what you would do there.

Telling a story from a book

Purpose: to asses the child's ability to recount a story from a picture book and to provide a context for comments about social relationships.
Materials and instruction: the child is asked to look at the book and asked to tell the story as they go along.
Substitutions for visually impaired children: the child is told of the central characters and the scene and is asked to tell a story about them.

7. Cartoons.

Optional.

8. Conversation and Reporting

Purpose: to assess the ability to engage and participate in conversation with a reciprocal nature.
Instructions: Child can be asked to describe a non routine event

9. Emotions

Interview questions

10. Social difficulties and annoyance

Interview questions

11. Break.

12. Friends and marriage.

Interview questions

13. Loneliness.

Interview questions

14. Creating a Story

Purpose: observe creativity
Materials: six items with a definite purpose and six items with no definite purpose
Instructions: the examiner tells the child that they are going to make up some stories using the objects. The participant is asked to use five items.
Substitutions for visually impaired children:

- Child is told what each item is, they are then asked to choose a character first. and pick four items.

Coding

Code 0 – behaviour shows no presence of abnormality
Code 1 – behaviour is mildly abnormal or slightly unusual.
Code 2 – behaviour is definitely abnormal.
Code 3 – behaviour markedly abnormal
Code 7 – when there is an abnormal behaviour of a type that is not encompassed by other ratings.
Code 8- the behaviour in question did not occur.

Coding for this module is separated into a language and communication, reciprocal social interaction, play and stereotyped behaviours and restricted behaviour.

Application of results

Diagnostic algorithms are sets of rules which allow classification of participants as having social and communicative deficits of autism or autism spectrum disorder. Diagnostic classification is made on the basis of exceeding the threshold on each of the two domains – social interaction and communication. (Computation and procedures are similar to that of DSM-IV).

Once the ADOS protocol has been scored, individual item ratings are copied onto the algorithm form provided for each subject. Thresholds for autism and for ASD are applied to each of the domain scores and the total score.

Some coding will need to be adapted to make allowances for children who are
Visually impaired, below the table will be used for a guideline for doing so.

Table 3.5: Changes to algorithm scores of the ADOS items, which relied heavily on vision

Module one		
Coding	**Original**	**Adapted**
A2 Frequency of vocalisation directed to other	0 = Directs vocalisations to parent/caregiver or examiner in a variety of context. Must include chatting or vocalisations to be friendly or to express interests, as well as t make needs known	0 = ~~Directs~~ vocalisations to parent/caregiver or examiner in a variety of context. Must include chatting or vocalisations to be friendly or to express interests, as well as t make needs known
	1 = Directs vocalisations to parent/caregiver or examiner consistently in one context, OR directs vocalisations to parent/caregiver across a variety of contexts	1 = ~~Directs~~ vocalisations to parent/caregiver or examiner consistently in one context, OR directs vocalisations to parent/caregiver across a variety of contexts
	2 =~~Directs~~–occasional vocalisation to parent/caregiver or examiner inconsistently in a limited number of contexts. May include whining or crying due to frustration	2 =~~Directs~~ occasional vocalisation to parent/caregiver or examiner inconsistently in a limited number of contexts. May include whining or crying due to frustration
	3= vocalisation almost never appears to be direct to parent/caregiver or examiner, OR rarely or never vocalises	3= vocalisation almost never appears to be direct to parent/caregiver or examiner, OR rarely or never vocalises
A6: Use of others body to communicate	0= No use of another person's body to communicate, except in situations where or other strategies have not worked (e.g, when others are conversing and the child cannot get their attention) and in conjunction with coordinated gaze	0= No use of another person's body to communicate, ~~except~~ **OR**, in situations where or other strategies have not worked (e.g., when others are conversing and the child cannot get their attention) and in conjunction with coordinated gaze or **appropriate vocalisation**
	1 = Take another person's hand and leads him/her places without coordinated gaze, but no placement of hand on objects and no use of it as a tool or to point	1 = Take another person's hand and leads him/her places without coordinated gaze or **appropriate vocalisation**, but no placement of hand on objects and no use of it as a tool or to point
	2 = Placement of another person's hand on object, OR movement of that person's hand when it is holding an object, OR use of his/her hand or other body part as a tool or to gesture	2 = Placement of another person's hand on object, OR movement of that person's hand when it is holding an object, OR use of his/her hand or

	"for" child the child (such as pointing	other body part as a tool or to gesture "for" child the child (such as pointing).
	8 = little or no spontaneous communication	8 = little or no spontaneous communication
A7:Pointing	0 = Points with index finger to show visually-directed referencing (co-ordinated gaze to object and person) of distal objects in at least two contexts	0 score for the blind
	1 = Uses pointing to reference objects, but without sufficient flexibility or frequency to meet criteria for a rating of 0 (e.g., only one instance of pointing that fits preceding description for a 0 rating, or absence of coordinated gaze with distal pointing, through the child may vocalise); OR produces an approximation of pointing rather than an index finger point; OR coordinates only pointing that includes touching a picture or other nearby objects with gaze or vocalisations; OR points only to a person or to himself/herself.	0 score for the blind
	2 = Points only when close to or actually touching an object, without coordinated gaze or vocalisation	0 score for the blind
	3= Does not point to objects to any way	0 score for the blind
B1: Unusual eye contact	0= Appropriate gaze with subtle changes meshed with other communication	0 score for the blind
	2 – Uses poorly modulated eye contact to initiate, terminate, or regulate social interaction	0 score for the blind
B2: Responsive social smile	0= Smiles immediately in response to one of the first two smiles of the examiner and/or parent/caregiver. This must be a clear change from non smiling to a fully responsive smile that is not prompted by a specific request (e.g. "give me a smile)	0= Smiles immediately in response to one of the first two smiles **or positive vocalisations** of the examiner and/or parent/caregiver. This must be a clear change from non smiling to a fully responsive smile that is not prompted by a specific request (e.g. "give me a smile)
	1 = Delayed or partial smile, OR smiles fully or partially only after more than two smiles by the parent/caregiver or the examiner, or smiles only in response to a specific request	1 = Delayed or partial smile, OR smiles fully or partially only after more than two smiles **or positive vocalisations** by the parent/caregiver or the examiner, or smiles only in response to a specific request

	2 = Smiles fully or partially at the parent/ caregiver or the examiner only after being tickled or touched in some way, OR in response to a repeated action with a physical component (even if the child is not actual touched	No change
	3 = Does not smile in response to another person	No change
B3: Facial Expression Directed to others	0 = Directs a range of appropriate facial expressions towards parent/caregiver or examiner in order to communicate affect	0 = Directs a range of appropriate facial expressions towards parent/caregiver or examiner in order to communicate affect. **Facial expression does not have to be directed to other, but can be towards source of sound, with definite change in expression , and body can be rotated to source of sound or examiner. Parent/caregiver**
	1 = Some direction of facial expression to examiner and/or parent/caregiver (e.g., directs only expressions indicating emotional extremes to others, or occasionally directs wider range of expression). A child who has slightly unusual facial expressions, but directs most of his/her facial expression to another person may be scored here	1 = Some direction of facial expression to examiner and/or parent/caregiver (e.g., directs only expressions indicating emotional extremes to others, or occasionally directs wider range of expression). A child who has slightly unusual facial expressions, but directs most of his/her facial expression to another person may be scored here. **Facial expression does not have to be directed to other, but can be towards source of sound, with definite change in expression but to extremes, and body can be rotated to source of sound or examiner. Parent/caregiver**
	2 = Rarely or never directs appropriate facial expression to others	No change
B4: Intergradations of Gaze and other behaviours during social overtures	0 = uses eye contact effectively with words or vocalisation or gestures to communicate	0 = uses ~~eye contact~~ **physical contact or change in body orientation towards examiner, parent/caregiver** contact effectively with words or vocalisation or gestures to communicate
	1 = uses eye contact and vocalisations independently of each	1 = uses ~~eye contact~~, **physical** contact, or **body**

	other to communicate social intention (i.e., uses both eye contact and other strategies at different times, but does not coordinate them with each other)	**orientation towards examiner, parent/caregiver** and vocalisations independently of each other to communicate social intention (i.e., uses both eye contact and other strategies at different times, but does not coordinate them with each other)
	2 = uses either eye contact or vocalisations to communicate social intention	2 = uses either ~~eye-contact~~ **physical** contact, or **body orientation towards examiner, parent/caregiver** or vocalisations to communicate social intention
	3 = uses neither eye contact nor vocalisations to communicate social intention Or no social overtures	3 = uses neither ~~eye-contact~~, **physical** contact, or **body orientation towards examiner, parent/caregiver** nor vocalisations to communicate social intention Or no social overtures
B6: Response to Name	0 = Looks toward the examiner and makes eye contact immediately on at least one of the first two clear presses made by the examiner (i.e., name only is called)	0 = **Orientates body** ~~Looks~~ toward the examiner and **stills** ~~makes eye contact~~ immediately on at least one of the first two clear presses made by the examiner (i.e., name only is called)
	1 = Looks toward the parent/caregiver and makes eye contact immediately for first or second press of name only, OR makes eye contact with the examiner immediately for the examiner's third or fourth press of name only	1 = **Orientates body** ~~Looks~~ toward the parent/caregiver and makes **stills** ~~eye-contact~~ immediately for first or second press of name only, OR makes eye contact with the examiner immediately for the examiner's third or fourth press of name only
	2 = Does not make eye contact with either the examiner or the parent/caregiver after his/her name is called in six attempts, but shifts gaze briefly (no eye contact), OR looks at least one when an interesting or familiar vocalisations or verbalisation is made (e.g., tongue clucking; " gonna get you")	2 = Does not **orientate body toward** ~~make eye contact~~ with either the examiner or the parent/caregiver after his/her name is called in six attempts, but **orientate body** ~~shifts gaze~~ briefly ~~(no eye contact)~~, OR **turns towards very briefly** ~~looks at least once when~~ **to** an interesting or familiar vocalisations or verbalisation is made (e.g., tongue clucking; " gonna get you")

	3 = Does not look toward either the examiner or the parent/caregiver after any purely verbal or vocal attempt to get attention	3 = Does not **orientate body** ~~look~~ toward either the examiner or the parent/caregiver after any purely verbal or vocal attempt to get attention
B7: Requesting	0 = Exhibits appropriate integration of eye contact and at least one behaviour (e.g. vocalisation, gesture or handing an object to the examiner or the parent giver) to request bubbles, the switch operated animal, object routine, or social routine. Must include eye contact and a definite indication of wanting the other person to do or give something (e.g., by persisting in the request if the other person pauses before responding). This does not include physically pulling or placing the examiner's hand onto an object or to the child himself/herself.	0= Exhibits appropriate integration of ~~eye contact and at least one behaviour (e.g.~~ vocalisation, gesture or handing an object to the examiner or the parent giver~~)~~ to request bubbles, the switch operated animal, object routine, or social routine. Must include ~~eye contact and~~ a definite indication of wanting the other person to do or give something (e.g., by persisting in the request if the other person pauses before responding). This does not include physically pulling or placing the examiner's hand onto an object or to the child himself/herself.
B9 Showing	0 = Spontaneously shows toys or objects throughout the ADOS evaluation by holding them up or placing them in front of others and using eye contact with or without vocalisation	0 = Spontaneously shows toys or objects throughout the ADOS evaluation by holding them up or placing them in front of others ~~and using eye contact~~ with or without vocalisation includes handing object over, or intent to gage intention to show, though physical contact. **Attempts to include examiner in object and interaction, but not to use examiner as tool to operate toy, must to be a reciprocal.**

	1 = Shows toys or objects in a partial or inconsistent manner (e.g., holds them up and/or places them in front of others without coordinated eye contact, looks from an object in his/her hands to another person without clearly orientating it toward that person, or shows objects as described above for a 0 rating on one occasion.	1= Shows toys or objects in a partial or inconsistent manner (e.g., holds them up and/or places them in front of others **without attempts to include examiner in object and interaction** ~~without coordinated eye contact, looks from an object in his/her hands to another person without clearly orientating it toward that person, or shows objects as described above for a 0 rating on one occasion~~

Module Two		
Coding	**Original**	**Adapted**
A7 = Pointing		0 score for the blind
B1 = Unusual eye contact		0 score for the blind
B4= Response to name	0 = Looks toward the examiner and makes eye contact immediately on at least one of the first two clear presses made by the examiner (i.e., name only is called)	0 = **Orientates body** ~~Looks~~ toward the examiner and **stills** ~~makes eye contact~~ immediately on at least one of the first two clear presses made by the examiner (i.e., name only is called)
B5 = Showing	0 = Spontaneously shows toys or objects throughout the ADOS evaluation by holding them up or placing them in front of others and using eye contact with or without vocalisation	0 = Spontaneously shows toys or objects throughout the ADOS evaluation by holding them up or placing them in front of others ~~and using eye contact~~ with or without vocalisation includes handing object over, or intent to gage intention to show, though physical contact. **Attempts to include examiner in object and interaction, but not to use examiner as tool to operate toy, must to be a reciprocal.**
B6 =Spontaneous initiation of joint attention		0 score for the blind
B7 = Response to joint attention		0 score for the blind
Module Three and Module Four		
Coding	**Original**	**Adapted**
B1 = unusual eye contact		0 score for the blind

APPENDIX D: PARENTAL INFORMATION PACK

Dear Parents,

My name is Jagjeet Jutley, I am currently studying for my PhD at the University of Birmingham in conjunction with Birmingham Children's hospital.

The Focus Family group has kindly agreed to distribute information about the research I am conducting, on my behalf, to its members

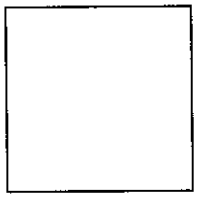
I would like to invite you to take part in research which looks at the types of social and communicative behaviours seen in children
with Septo-Optic Dysplasia, Optic, Nerve Hypoplasia and isolated" hypopituitarism.

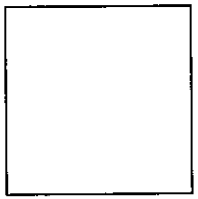
I have enclosed an information sheet which explains more about the study and what will happen if you agree to take part. Please take some time to read this carefully. If you would like to participate please sign the consent form enclosed with this letter and return to me in the prepaid envelope provided.

If you have any questions about this research please feel free to contact me via e-mail (JKJ579@bham.ac.uk) or telephone ( )

Yours Faithfully

Jagjeet Jutley
Postgraduate research





Invitation and Information Sheet for parent/carer

Investigation into the identification of social and communicative behaviours of children with isolated hypopituitarism

You are being invited to take part in a research study. Before you decide whether or not to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

The research study is being conducted by Jagjeet Jutley (BSc, MRes), from the School of Psychology at the University of Birmingham and Birmingham Children's Hospital's Endocrinology Department as part of an educational project for the researcher's PhD.

What is the purpose of the study?

You have been invited to take part in the study because your child has been diagnosed as having "isolated" hypopituitarism, which refers to an absence or reduction of one of the six hormones produces by the anterior pituitary gland. The aim of the study is to investigate the social and communicative behaviours of children with "isolated" hypopituitarism because research studies have yet to examine this.

All tasks will be based on play and educational situations using toys and pretend play activities which aim to elicit social communicative responses from your child. The activities should be enjoyed by your child.

Do I have to take part?

It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form which is enclosed. If you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care your child receives.

What does it involve?

Currently, it is anticipated seventy-five participants will take part in the study, which will run over the course of three years, but assessments will

be carried out over one year. During the first six months, two sessions of formal assessments of your child's social and communicative behaviour will be carried out. A researcher who is formally trained on assessing these behaviours in children will study your child's development, by observing your child's performance on play tasks with the researcher.

These tests will take approximately one hour and will be carried out at your child's school, home, or at the university, whichever is the more convenient for you. During the assessment you are free to join in with the play activities and you will be briefed on what the tests involve before the researcher commences. A further one hour session with yourself will be scheduled to complete questionnaires relating to your child's social development and a general development.

Are there any benefits?

This will be the first study to investigate social and communicative behaviours in children with "isolated" hypopituitarism. It may help to improve the identification of children who may require additional learning resources and appropriate behavioural interventions, which may support in your child's future development. It may explain any inconsistencies in previous behaviours to parents and caregivers. It may give you new ideas of how to encourage social and communicative skills in your child, which may benefit your child's social development.

What are the Potential risks and discomforts?

There are no foreseen risks. Parents/guardians are free to be present during assessments.

Financial obligations

There are no financial obligations and any travel expenses will be reimbursed.

Privacy and confidentiality

All information which is collected about your child during the research will remain completely confidential and can only be accessed by the researcher, Dr J. Kirk and Dr G. Harris. Tests will be videotaped in order for the researcher to analyse the data which has been collected. The tapes will be stored in a lockable filling cabinet at the university. On completion of the research study, tapes will be kept for a further three years and then destroyed.

What will happen to the results of the research study?

We will tell you what happens to the results of the research, when they are likely to be published, where you can obtain a copy of the published results. At the end of study you will be provided with a summary sheet of the research. Additionally, an individualised summary of your child's performance will be provided for you and your child. You and your child will not be identified in anything that is published. Any data kept about

your child will be coded by numbers rather than names.

Who is organising and funding the research?

The study is being organised by the Birmingham Children's Hospital and the University of Birmingham and has been sponsored by Dr Jeremy Kirk of the Endocrinology Department and Dr Gillian Harris from the University of Birmingham.

What happens if I decide to take part?

Please complete the attached consent form and return it, in the pre-paid envelope provided. There are two copies, one for you to keep and one to be sent off.

Has the proposed researched been reviewed?

The study has been reviewed by the South Birmingham Ethic Committee.

For Further questions please contact:

If you have any other questions or require further details on the research, feel free to contact **Jagjeet Jutley** at the following address:

School of Psychology
University of Birmingham
Birmingham
B12 2TT

Supervisor Details: Dr Gill Harris

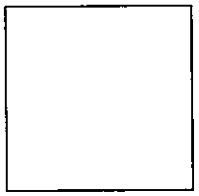
School of Psychology
University of Birmingham

Birmingham
B12 2TT
Tel: 0121 414 4934
Email: g.harris@bham.ac.uk

Thank you very much for your time.

Yours Faithfully

Jagjeet Jutley (BSc, MRes



Invitation and Information Sheet
for parent/carer

INVESTIGATING THE IDENTICATION OF SOCIAL AND COMMUNICATIVE BEHAVIOURS IN CHILDREN WITH OPTIC NERVE HYPOPLASIA

You are being invited to take part in a research study. Before you decide whether or not to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

The research study is being conducted by Jagjeet Jutley (BSc, MRes), from the School of Psychology at the University of Birmingham and Birmingham Children's Hospital's Endocrinology Department as part of an educational project for the researcher's PhD.

What is the purpose of the study?

You have been invited to take part in the study because your child has been diagnosed as having small nerves leading from the brain to the eyes; Optic Nerve Hypoplasia (ONH). The aim of the study is to investigate the social and communicative behaviours of children with ONH because research studies have yet to examine this.

All tasks will be based on play and educational situations using toys and pretend play activities which aim to elicit social communicative responses from your child. The activities should be enjoyed by your child. If you are concerned about your child's development, you will have an opportunity for a referral to a Clinical Psychologist at the Birmingham Children's Hospital to address care plan for your child.

Do I have to take part?

It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form which is enclosed. If you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care your child receives.

What does it involve?

A Formal assessment of your child's social and communicative behavior will be carried out. A researcher who is trained on assessing these behaviours in children will study your child's development, by observing your child's performance on play tasks with the researcher. Also, a short screening test of verbal intelligence which will look at your child's vocabulary, memory, arithmetic and comprehension will be administered.

These tests will take approximately one - two hour and will be carried out at your child's school, home, or at the university, whichever is the more convenient for you. I will send questionnaires for you to complete relating to your child's social development and a general development.

Are there any benefits?

This will be the first study to investigate the social and communicative behaviours of children with Optic Nerve Hypoplasia (ONH). It may help to improve the identification of children who may require additional learning resources and appropriate behavioural interventions which may support in your child's future development. It may explain any inconsistencies in

previous behaviours to parents and caregivers. It may give you new ideas of how to encourage social and communicative skills in your child, which may benefit your child's social development.

What are the Potential risks and discomforts?

There are no foreseen risks. Parents/guardians are free to be present during assessments.

Financial obligations

There are no financial obligations and any travel expenses will be reimbursed.

Privacy and confidentiality

All information which is collected about your child during the research will remain completely confidential and can only be accessed by the researcher, Dr J. Kirk and Dr G. Harris. Tests will be videotaped in order for the researcher to analyse the data which has been collected. The tapes will be stored in a lockable filling cabinet at the university. On completion of the research study, tapes will be kept for a further three years and then destroyed.

What will happen to the results of the research study?

We will tell you what happens to the results of the research, when they are likely to be published, where you can obtain a copy of the published results. At the end of study you will be provided with a summary sheet of the research. You and your child will not be identified in anything that is published. Any data kept about your child will be coded by numbers rather than names.

Who is organising and funding the research?

The study is being organised by the Birmingham Children's Hospital and the University of Birmingham and has been sponsored by Dr Jeremy Kirk of the Endocrinology Department and Dr Gillian Harris from the University of Birmingham.

What happens if I decide to take part?

Please complete the attached consent form and return it, in the pre-paid envelope provided. There are two copies, one for you to keep and one to be sent off.

Has the proposed researched been reviewed?

The study has been reviewed by the South Birmingham Ethic Committee.

For Further questions please contact:

If you have any other questions or require further details on the research, feel free to contact **Jagjeet Jutley** at the following address:

School of Psychology
University of Birmingham
Birmingham
B12 2TT
Tel: 0121 414 3507
Email: jkj379@bham.ac.uk

Supervisor Details: Dr Gill Harris

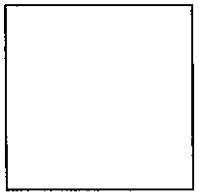
School of Psychology
University of Birmingham

Birmingham
B12 2TT
Tel: 0121 414 4934
Email: g.harris@bham.ac.uk

Thank you very much for your time.

Yours Faithfully

Jagjeet Jutley (BSc, MRes



Invitation and Information Sheet for parent/carer

INVESTIGATING THE IDENTICATION OF SOCIAL AND COMMUNICATIVE BEHAVIOURS IN CHILDREN WITH SEPTO OPTIC DYSPLASIA.

You are being invited to take part in a research study. Before you decide whether or not to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

The research study is being conducted by Jagjeet Jutley (BSc, MRes), from the School of Psychology at the University of Birmingham and Birmingham Children's Hospital's Endocrinology Department as part of an educational project for the researcher's PhD.

What is the purpose of the study?

You have been invited to take part in the study because your child has been diagnosed with Septo-Optic Dysplasia (SOD). Your child will exhibit at least two of three following: structural brain lesions, hormonal deficiency(s) and/or small nerves leading from the brain to the eyes; so called Septo Optic Dysplasia. The aim of the study is to investigate the social and communicative behaviours of children with SOD as research studies have yet to examine this.

All tasks will be based on play and educational situations using toys and pretend play activities which aim to elicit social communicative responses from your child. The activities should be enjoyed by your child.

Do I have to take part?

It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form which is enclosed. If you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care your child receives.

What does it involve?

A Formal assessment of your child's social and communicative behavior will be carried out. A researcher who is trained on assessing these behaviours in children will study your child's development, by observing your child's performance on play tasks with the researcher. Also, a short screening test of verbal intelligence which will look at your child's vocabulary, memory, arithmetic and comprehension will be administered.

These tests will take approximately one - two hour and will be carried out at your child's school, home, or at the university, whichever is the more convenient for you. I will send questionnaires for you to complete relating to your child's social development and a general development.

Are there any benefits?

This will be the first study to investigate the social and communicative behaviours of children with Septo Optic Dysplasia (SOD). It may help to improve the identification

of children who may require additional learning resources and appropriate behavioural interventions which may support in your child's future development. It may explain any inconsistencies in previous behaviours to parents and caregivers. It may give you new ideas of how to encourage social and communicative skills in your child, which may benefit your child's social development.

What are the Potential risks and discomforts?

There are no foreseen risks. Parents/guardians are free to be present during assessments.

Financial obligations

There are no financial obligations and any travel expenses will be reimbursed.

Privacy and confidentiality

All information which is collected about your child during the research will remain completely confidential and can only be accessed by the researcher, Dr J. Kirk and Dr G. Harris. Tests will be videotaped in order for the researcher to analyse the data which has been collected. The tapes will be stored in a lockable filling cabinet at the university. On completion of the research study, tapes will be kept for a further three years and then destroyed.

What will happen to the results of the research study?

We will tell you what happens to the results of the research, when they are likely to be published, where you can obtain a copy of the published results. At the end of study you will be provided with a summary sheet of the research. Additionally, an individualised summary of your child's performance will be provided for you and your child. You and your child will not be identified in anything that is published. Any data kept about your child will be coded by numbers rather than names.

Who is organising and funding the research?

The study is being organised by the Birmingham Children's Hospital and the University of Birmingham and has been sponsored by Dr Jeremy Kirk of the Endocrinology Department and Dr Gillian Harris from the University of Birmingham.

What happens if I decide to take part?

Please complete the attached consent form and return it, in the pre-paid envelope provided. There are two copies, one for you to keep and one to be sent off.

Has the proposed researched been reviewed?

The study has been reviewed by the South Birmingham Ethic Committee.

For Further questions please contact:

If you have any other questions or require further details on the research, feel free to contact **Jagjeet Jutley** at the following address:

School of Psychology
University of Birmingham
Birmingham
B12 2TT

Supervisor Details: Dr Gill Harris

School of Psychology
University of Birmingham

Birmingham
B12 2TT
Tel: 0121 414 4934
Email: g.harris@bham.ac.uk

Thank you very much for your time.

Yours Faithfully

Jagjeet Jutley (BSc, MRes)

CONSENT/ASSENT FORM

INVESTIGATING THE IDENTICATION OF SOCIAL AND COMMUNICATIVE BEHAVIOURS IN CHILDREN WITH SEPTO OPTIC DYSPLASIA

Please tick to indicate:

- I have read and understood the information sheet provided for the above study. ☐
- I have been made aware of where and how to ask for further information before I give consent ☐
- I understand that my participation and my child's participation are purely voluntary. I understand I can withdraw at any time, without giving reason and without my child's care or legal rights being affected. ☐
- I give consent for my child's GP to be informed of our participation in the research study YES/NO (please circle)
- I give consent for me, and assent for my child, to take part in the research project. ☐

_____ Name of child

_____ Name of parent

_____ Signature of parent

_____ Date

Signature of Principal Investigator: for office use only

_____ Name of principal investigator

_____ Signature of investigator

_____ Date

CONSENT/ASSENT FORM

INVESTIGATING THE IDENTICATION OF SOCIAL AND COMMUNICATIVE BEHAVIOURS IN CHILDREN WITH OPTIC NERVE HYSPOPLASIA

Please tick to indicate:

- I have read and understood the information sheet provided for the above study. ☐
- I have been made aware of where and how to ask for further information before I give consent ☐
- I understand that my participation and my child's participation are purely voluntary. I understand I can withdraw at any time, without giving reason and without my child's care or legal rights being affected. ☐
- I give consent for my child's GP to be informed of our participation in the research study YES/NO (please circle)
- I give consent for me, and assent for my child, to take part in the research project. ☐

_____ _____

Name of child Name of parent

_____ _____

Signature of parent Date

Signature of Principal Investigator: for office use only

_____

Name of principal investigator

_____ _____

Signature of investigator Date

CONSENT/ASSENT FORM

INVESTIGATING THE IDENTICATION OF SOCIAL AND COMMUNICATIVE BEHAVIOURS IN CHILDREN WITH ISOLATED HYPOPITUTARISM

Please tick to indicate:

- I have read and understood the information sheet provided for the above study. ☐
- I have been made aware of where and how to ask for further information before I give consent ☐
- I understand that my participation and my child's participation are purely voluntary. I understand I can withdraw at any time, without giving reason and without my child's care or legal rights being affected. ☐
- I give consent for my child's GP to be informed of our participation in the research study YES/NO (please circle)
- I give consent for me, and assent for my child, to take part in the research project. ☐

_____ Name of child

_____ Name of parent

_____ Signature of parent

_____ Date

Signature of Principal Investigator: for office use only

_____ Name of principal investigator

_____ Signature of investigator

_____ Date

Looking at how you like to play and talk to people

Invitation and information sheet for child participant

You are being invited to take part in a research study. Before you decide whether or not to take part, it is important for you to understand why the research is being done and what it will involve. Ask your parents or myself, if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

The research study is being conducted by Jagjeet Jutley (BSc, MRes), from the School of Psychology at the University of Birmingham and Birmingham Children's Hospital's Endocrinology Department as part of an educational project for the researcher's PhD.

Why are we doing this study?

You have been invited to take part in the study because you have problems with growing. (i.e. isolated hypopituitarism) Nobody has looked at the way a child with growth problems like to play and talk to people. This may be different to other children due to your growth problems.

Do I have to take part?

It is up to you to decide to take part or not. If you do decide to take part, keep this information sheet and sign the consent form, which is enclosed. If you decide to take part, you are still free to change your mind and you do not have to tell me why. If you decide not to take part, the care you receive from your doctors will not change.

For Further questions please contact

If you have any other questions or require further details on the research, feel free to contact **Jagjeet Jutley** at the following address:

School of Psychology
University of Birmingham
Edgbaston
Birmingham -

B12 2TT

Supervisor Details: Dr Gill Harris

School of Psychology
University of Birmingham
Edgbaston
Birmingham
B12 2TT
Tel: 0121 414 4934 (during office hours)

Email: g.harris@bham.ac.uk

Thank you very much for your time.

Yours Faithfully

Jagjeet Jutley

What does it involve?

75 children with growth problems will hopefully take part in the study and your participation will be for about one year. I will visit you first to play with some toys, read books and talk to you about what you like to do and any places you have been to visit which you have enjoyed. Secondly, I will ask you some questions about words and numbers. It will take about one –two hours and we can do this at your school, home, or at the university or hospital, whichever is the better for you.

Privacy and Confidentiality

All information, which is collected, about you during the research will remain completely confidential and can only be accessed by the researcher, Dr J. Kirk and Dr G. Harris. I will videotape my visits with you and the tapes will be stored in a locked cabinet at the university. Once I have finished the research study I will keep the tapes for a further three years and then destroy them

What will happen to the results of the research study?

I will tell you what happens to the results of the research. At the end of study, you will be provided with a summary sheet of the research. Additionally, an individualised summary of your performance will give to you.

What happens if I decide to take part?

Please complete the attached consent form and return it, in the pre-paid envelope provided. There are two copies, one for you to keep and one to be sent off.

Looking at how you like to play and talk to people

Invitation and information sheet for child participant

You are being invited to take part in a research study. Before you decide whether or not to take part, it is important for you to understand why the research is being done and what it will involve. Ask your parents or myself, if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

The research study is being conducted by Jagjeet Jutley (BSc, MRes), from the School of Psychology at the University of Birmingham and Birmingham Children's Hospital's Endocrinology Department as part of an educational project for the researcher's PhD.

Why are we doing this study?

All information, which is collected, about you during the research will remain completely confidential and can only be accessed by the researcher, Dr J. Kirk and Dr G. Harris. I will videotape my visits with you and the tapes will be stored in a locked cabinet at the university. Once I have finished the research study I will keep the tapes for a further three years and then destroy them

What will happen to the results of the research study?

I will tell you what happens to the results of the research. At the end of study, you will be provided with a summary sheet of the research. Additionally, an individualised summary of your performance will give to you.

What happens if I decide to take part?

Please complete the attached consent form and return it, in the pre-paid envelope provided. There are two copies, one for you to keep and one to be sent of

Looking at how you like to play and talk to people

Invitation and information sheet for child participant

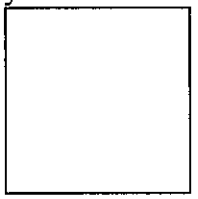
You are being invited to take part in a research study. Before you decide whether or not to take part, it is important for you to understand why the research is being done and what it will involve. Ask your parents or myself, if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part. The research study is being conducted by Jagjeet Jutley (BSc, MRes), from the School of Psychology at the University of Birmingham and Birmingham Children's Hospital's Endocrinology Department as part of an educational project for the researcher's PhD.

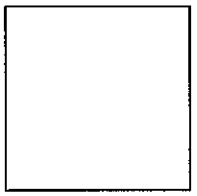
Why are we doing this study?

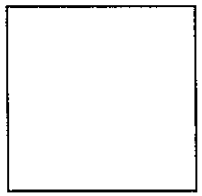
You have been invited to take part in the study because you may have problems with growing, and/or your eyesight and/or development. (i.e. Septo-optic dysplasia) Nobody has looked at the way a child with septo - optic dysplasia likes to play and talk to people, as this may be different to other children due to your condition.

Do I have to take part?

it is up to you to decide to take part or not. If you do decide to take part, keep this information sheet and sign the consent form, which is enclosed. If you decide to take part, you are still free to change your mind and you do not have to tell me why. If you decide not to take part, the care you receive from your doctors will not change.







For Further, questions please contact

If you have any other questions or require further details on the research, feel free to contact **Jagjeet Jutley** at the following address:

School of Psychology
University of Birmingham
Edgbaston
Birmingham

B12 2TT

Supervisor Details: Dr Gill Harris

School of Psychology
University of Birmingham
Edgbaston
Birmingham
B12 2TT
Tel: 0121 414 4934 (during office hours)
Email: g.harris@bham.ac.uk

Thank you very much for your time.
Yours Faithfully

Jagjeet Jutley

What does it involve?

I will visit you first to play with some toys and talk to you about what you like to do and any places you have been to visit which you have enjoyed. Secondly, I will ask you some questions about numbers and words. It will take about one – two hours and we can do this at your school, home, or at the university or hospital, whichever is the better for you.

Privacy and Confidentiality

All information, which is collected, about you during the research will remain completely confidential and can only, be accessed by the researcher, Dr J. Kirk and Dr G. Harris. I will videotape my visits with you and the tapes will be stored in a locked cabinet at the university. Once I have finished the research study I will keep the tapes for a further three years and then destroy them

What will happen to the results of the research study?

I will tell you what happens to the results of the research. At the end of study, you will be provided with a summary sheet of the research. Additionally, an individualised summary of your performance will give to you.

What happens if I decide to take part?

Please complete the attached consent form and return it, in the pre-paid envelope provided. There are two copies, one for you to keep and one to be sent off.

CHILD CONSENT FORM INVESTIGATING THE SOCIAL AND COMMUNICATIVE BEHAVIOURS OF CHILDREN WITH OPTIC NERVE HYPOPLASIA

Please ask your parent/carer to explain anything to you that you do not understand or you can contact me with details provided on the information sheet.

Please tick to indicate you have understood the following statements and sign if you agree to participate in the study.

- I have read and understood the information sheet provided for the above study. ☐
- I have been explained where and how to ask for furthering formation before I give consent ☐
- I understand that my participation is voluntary; I withdraw at any time, without giving reason and without my care or legal rights being affected. ☐
- I give consent for my GP to be informed of my Participation in the research study
- I give consent for to take part in the research project. ☐

Please sign below if everything about the study has been understood by you:

Your name _____

CHILD CONSENT FORM INVESTIGATING THE SOCIAL AND COMMUNICATIVE BEHAVIOURS OF CHILLDREN WITH SEPTO OPTIC DYSPLASIA

Please ask your parent/carer to explain anything to you that you don't understand or you can contact me with details provided on the information sheet.

Please tick to indicate you have understood the following statements and sign to agree to participate in the study.

- I have read and understood the information sheet provided for the above study. ☐
- I have been explained where and how to ask for furthering formation before I give consent ☐
- I understand that my participation is voluntary; I withdraw at any time, without giving reason and without my care or legal rights being affected.
- I give consent for my GP to be informed of my Participation in the research study ☐
- I give consent for to take part in the research project. ☐

Please sign below if everything about the study has been understood by you:

Your name _____

CHILD CONSENT FORM
INVESTIGATING THE SOCIAL AND COMMUNICATIVE BEHAVIOURS OF CHILDREN WITH ISOLATED HYPOPITUITARISM

Please ask your parent/carer to explain anything to you that you don't understand or you can contact me with details provided on the information sheet.

Please tick to indicate you have understood the following statements and sign to agree to participate in the study.

- I have read and understood the information sheet provided for the above study. ☐
- I have been explained where and how to ask for furthering formation before I give consent ☐
- I understand that my participation is voluntary; I withdraw at any time, without giving reason and without my care or legal rights being affected.
- I give consent for my GP to be informed of my Participation in the research study ☐
- I give consent for to take part in the research project. ☐

Please sign below if everything about the study has been understood by you:

Your name _____

In regards to:

CONFIDENTIAL

Dear,

Subject: Research on Septo Optic Dysplasia

-------- is taking part in a research project funded by the Birmingham Children's hospital's Endocrinology Department and the University Of Birmingham's School Of Psychology. The research will form part of an educational project for a PhD.

We are looking at the social and communicative behaviours, general developmental abilities and behaviours of children with Septo Optic Dysplasia. Tasks are based on play situations and educational activities adapted for children with visual impairments. Currently we are recruiting in the midlands area and anticipate 25 patients with ONH to participate.

What is involved for the School and -----?

I will visit ----- for 45 minutes on two separate occasions (or together, whichever is convenient for the school). I will require a quiet room, two chairs and a table. It is entirely up to the school to designate an appropriate time for me to visit. I have enclosed my contact details, for you to contact me to arrange the visit(s) which suit the school or I will phone in fourteen days times to discuss the visit.

Privacy and Confidentiality

All information which is collected will remain confidential and formal consent forms have been signed by both the child and parent. There will be no mention of the school in any publications and all data (including videotape data) collected is stored in lockable cabinets which can only be accessed by the researcher. The research project has been reviewed and accepted by the NHS and South Birmingham Ethics Committee. I have enclosed an up to date CRB check and when I visit I will wear an NHS ID badge for identification purposes.

Thank you for your cooperation with the project. If you have any questions regarding the research project (or about Septo Optic Dysplasia), please do not hesitate to contact me on the details provided.

Best regards,

Miss Jagjeet Jutley (MRes & BSc)
Postgraduate Researcher

Contact details:
School of Psychology
Room 416, Frankland Building
University of Birmingham
Bristol Road
Birmingham

B15 1BR

08 February 2006

In regards to: / Research Project on Optic nerve hypoplasia

CONFIDENTIAL

Dear ----------,

I have enclosed a copy of a letter which I have sent to your child's school in regards to the present research project. I will commence assessments as soon as the school has provided me with dates for my visit, which I will make you aware of in writing.

Once I have gathered all the information from the assessments on your child's social and communicative behaviours I will send a summary of these findings to you. Once we have gathered all of the information from our participants, we will advise you of how to access the PhD and other publications. However, I will send a summary to you of the main research findings in the post at the end of my

regards,

Miss Jagjeet Jutley (MRes & BSc)
Postgraduate Researcher

Contact details:

School of Psychology
Room 416, Frankland Building
University of Birmingham
Bristol Road
Birmingham
B15 1BR

PARTICIPANTS NEEDED FOR RESEARCH LOOKING AT THE IDENTIFICATION OF THE TYPES OF SOCIAL AND COMMUNICATIVE BEHAVIOURS IN CHILDREN WITH SEPTO OPTIC DYSPLASIA, OPTIC NERVE HYPOPLASIA AND ISOLATED HYPOPITUITARISM.

Although not systematically investigated, anecdotal reports from clinicians and parents have noted higher incidences of autistic-type behaviours in children with the named syndromes above.

The aim of the current research is to investigate the presence, types and varying degrees of autistic behaviours in the three different groups of children and if these behaviours are truly autistic in origin or due to a child's visual impairment.

Would you like to take part?

The more people who take part in the research, the more reliable any findings will be. A better understanding of social impairments in children with visual impairments and/or intellectual disability should lead to better detection and interventions in the future.

I am looking for children aged between 4 -16 years of age.

What does it involve?

I will firstly send some questionnaires in the post for you to complete and send back to me.

Secondly, I will need to visit your child either at their school or your home, whichever is the more convenient for you, to carry out an assessment looking at behaviours which can be impaired in children with autistic spectrum disorders. The one hour assessment is based on play activities which are aimed to elicit social and communicative behaviours in your child by using toys and for older children there will be some questions to answer. I will also do a quick fifteen to thirty minute assessment looking at your child's general ability. Most of the children I have visited so far seem to quite enjoy themselves.

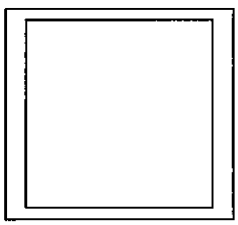
If you would like an information pack or have any questions please contact me by phone or e-mail and I will be happy to help.

Jagjeet Jutley

School of Psychology, University of Birmingham,

Edgbaston, Birmingham,

B15 2TT.



Appendix E

Table 6.6.3.1: Sensory Symptoms within subgroup of children with ONH/SOD with and without ASD according to SCQ Communication sub domain

Sensory Domain	Communication Domain	N	Mean	SD	χ^2	df	*P-value*
Tactile Sensitivity	-	19	30.47	6.65	42.25	2	. 29
	+	37	25.00	6.87			
Taste and Smell Sensitivity	-	19	15.68	5.67	65.12	2	.00
	+	37	13.68	6.12			
Movement sensitivity	-	19	14.62	6.27	23.76	2	.25
	+	37	12.77	3.01			
Under responsive Seeks sensation	-	19	24.59	8.57	35.04	2	.83
	+	37	19.50	6.93			
Auditory Filtering	-	19	21.00	6.76	50.7	2	.37
	+	37	18.82	5.64			
Low Energy	-	19	24.00	6.61	39.39	2	.67
	+	37	17.50	7.49			
Auditory Sensitivity	-	19	7.56	2.60	18.79	2	.28
	+	37	5.23	2.51			
Total Sensory Score	-	19	137.03	24.39	65.41	2	.93
	+	37	117.23	23.49			

(+) scoring above the cut-off for ASD, (-) scoring below the cut-off for ASD

Table 6.6.3.2: Sensory Symptoms within subgroup of children with ONH/SOD with and without ASD according to SCQ Reciprocal interaction sub domain

Sensory Domain	Reciprocal Interaction	N	Mean	SD	χ^2	Df	*P-value*
Tactile Sensitivity	-	36	30.56	6.49	42.25	2	.29
	+	20	24.30	6.78			
Taste and Smell Sensitivity	-	36	15.78	5.62	65.12	2	.00
	+	20	13.30	6.15			
Movement Sensitivity	-	36	14.53	6.10	23.76	2	.25
	+	20	12.75	3.16			
Under - responsive Seeks Sensation	-	36	24.42	8.47	22.86	2	.41
	+	20	19.30	7.10			
Auditory Filtering	-	36	7.25	2.69	35.31	2	.06
	+	20	5.55	2.68			
Low Energy	-	36	23.75	6.74	27.58	2	.19
	+	20	17.30	7.48			
Auditory	-	36	21.28	6.85	29.08	2	.02

Sensitivity	+	20	18.10	4.97			
Total Sensory Score	-	36	137.00	24.93	72.12	2	.82
	+	20	115.30	21.32			

(+) scoring above the cut-off for ASD, (-) scoring below the cut-off for ASD

Table 6.6.3.3: Sensory Symptoms within subgroup of children with ONH/SOD with and without ASD according to SCQ Stereotyped behaviours sub domain

Sensory Domain	Stereotyped Behaviours	N	Mean	SD	χ^2	Df	*P-value*
Tactile Sensitivity	-	32	31.06	6.63	50.95	2	.08
	+	23	24.39	6.18			
Taste and Smell Sensitivity	-	32	16.42	5.56	66.74	2	.00
	+	23	12.70	5.73			
Movement Sensitivity	-	32	14.52	6.00	27.29	2	.13
	+	23	13.00	4.00			
Under-responsive Seeks Sensation	-	32	25.21	8.48	38.25	2	.72
	+	23	18.83	6.48			
Auditory Filtering	-	32	21.39	6.79	53.93	2	.26
	+	23	18.35	5.39			
Low Energy	-	32	22.97	7.01	40.03	2	.64
	+	23	19.26	8.06			
Auditory Sensitivity	-	32	7.94	2.47	29.08	2	.02
	+	23	4.78	2.09			
Total Sensory Score	-	32	139.64	23.28	72.12	2	.82
	+	23	114.35	21.79			

(+) scoring above the cut-off for ASD, (-) scoring below the cut-off for ASD