

**ASSESSING THE COGNITIVE, BEHAVIOURAL AND PSYCHOSOCIAL PROFILE
OF CHILDREN WITH RUSSELL SILVER SYNDROME**

By

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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

University of Birmingham

October 2009

ABSTRACT

The main objective of this research was to create a better understanding of the long term cognitive, behavioural and psychosocial consequences for children with Russell Silver Syndrome (RSS), a syndrome characterised by being born Small for Gestational Age (SGA) and having short stature and phenotypical facial features.

Initially a systematic review was conducted including studies assessing cognitive and behavioural development of children born SGA at term. All studies assessed the profile of children with RSS, in comparison to a control group. The cognitive profile, behavioural , particularly ADHD profile and a study specifically assessing Autistic Spectrum Disorder (ASD), and psychosocial profile were assessed. The final study in this thesis assessed how others, peers and adults, viewed children with RSS phenotypical features.

The systematic review revealed that the trend for SGA children is increasing cognitive difficulties with increasing age, possibly as a consequence of neuro-cognitive deficits, including grapho-motor and hand eye coordination difficulties, which were observed at all ages.

Investigations comparing the cognitive abilities of a larger RSS group with those of an age matched control group revealed a cognitive disadvantage in RSS children and it was found, that children with RSS were having greater difficulties in spatial tasks than in other areas, possibly reflecting difficulties with the tasks, rather than a true spatial deficit.

RSS children were found to have more behavioural problems than the control children; with the biggest effect seen for symptoms of ADHD. RSS males were found to have symptoms of both hyperactivity and inattention, while in RSS females only inattention was reported as significant. Overall the incidence of ASD in children with RSS was found to be higher than in the control group, and higher than would be expected by chance in the general population. Those children with RSS that met criteria for ASD did not differ significantly on any other factor from the remainder of the RSS group.

While RSS children were found to view themselves as physically smaller than did the control children and were less satisfied with their height, they did not report that they felt physically different

in any other way. In turn there was no impact on their self esteem. The findings from the final study offer an explanation for these findings, as it was not found, on the whole, that peers and adults viewed children with RSS features as having different personality traits than did control children.

Overall the findings from this research were positive and have real life application. It was important that weaknesses, such as was found for spatial ability and hyperactivity and inattention are recognised.

What this research was not able to conclude conclusively was why these patterns of behaviour were observed and this offers future directions for the research

For Ben, thank you for all your unwavering support and understanding!

Acknowledgements

I would like to thank all the children and families that have taken part in this project and the Child Growth Foundation, particularly Jenny Child, for all their help and support and for funding this research.

I would also like to thank Dr Gill Harris, my supervisor, for her support throughout this research.

Finally, thank you Steve and Jag for helping me get through times of procrastination!

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Chapter 1

Literature Review

1.1 Aims of the literature review

This literature review will first give an overview of Russell Silver Syndrome (RSS) and where research with RSS children currently stands with emphasis on hypoglycaemia. The review will then go on to define Low Birth Weight (LBW), Small for Gestational Age (SGA) and Intra Uterine Growth Restriction (IUGR). A systematic review of the long term consequences of being born SGA has been conducted and can be seen in study 1 of this thesis.

The second part of this review includes a summary of the behavioural disorders which will be covered in this thesis, ADHD and Autistic Spectrum Disorder, outlining the causes of these disorders and any links they might have with low birth weight.

The final part of the review covers areas which are relevant to the psychosocial development of children with RSS; short stature and baby faced facial appearance, assessing the potential consequences these could have for the RSS child.

The aim of this review is to provide a background understanding of RSS but also to support the research of this thesis, which attempts to create a cognitive, behavioural and psychosocial profile of children with RSS. As there is known to be an extent of heterogeneity in RSS syndrome, the literature review will also review potential causes for cognitive difficulties, behavioural problems and psychosocial functioning difficulties. Doing this will allow for a better understanding of why some RSS children may have more difficulties than others, in fact it may be impossible to arrive at a strict profile for all RSS children, but potentially risk factors for difficulties in this group could be detected.

1.2 Introduction to Russell Silver Syndrome

Russell Silver Syndrome (RSS), also known as Silver-Russell Syndrome (SRS), is a heterogeneous congenital disorder. It occurs in 1 in 50, 000 and 1 in 100,000 births (Anderson, Viskochil, O’Gorman & Gonzales, 2002; Perkins & Hoang-Xuan, 2002) with no racial bias. It is characterised by low birth weight due to intrauterine growth restriction (IUGR), continued short stature and facial dysmorphology (large forehead tapering to a small jaw). The predicted adult height of children with RSS without growth hormone treatment, is 149.5-153.5cm for males (-3.2SD) and

138 -147cm for females (-2.5SD) (Tanner, Lejarraga & Cameron, 1975; Wollmann, Kirchner, Enders, Preece & Ranke, 1995).

This section outlines a brief history of RSS, research of the potential genetics of RSS, an outline of the RSS diagnostic criteria, and a review of a known potential consequence including hypoglycaemia.

1.2.1. History of Russell Silver Syndrome

American researchers Silver, Kiaysu, George and Deamer (1953), were the first researchers to describe children displaying symptoms of what is now known as Russell Silver Syndrome (RSS). The two children reported were small at birth and did not display postnatal catch up growth. Both cases displayed body asymmetry and a skull which appeared large for the size of their body, one child also displayed clinodactyly, incurving, of the little finger and the other a café au lait patch on the abdomen. Silver et al., (1953) attempted to relate these findings to descriptions of other disorders, such as ovarian agenesis, with little success.

In 1954 Russell, a British researcher, presented five cases of children with symptoms similar to those seen in the children reported by Silver et al., (1953). All five of the children described by Russell (1954) displayed 'dwarfism', attributed to an intra-uterine cause, and showed a characteristic face shape with a large forehead and small chin. The mouths of these children were described as 'drawn down at the sides' and all displayed clinodactyly of the little finger. All of the children were thin, with two displaying body asymmetry. Russell (1954) had monitored the children's growth over a number of years and reported that their lengths remained 3-4 inches, and their weights 6lbs, below the 3rd centile for appropriate age. Investigations by Russell (1954) failed to find a definitive cause for this apparent syndrome, and he urged that the case of these children be defined as a new syndrome. The observations of Silver et al., (1953) and Russell (1954) were the first reported cases of the syndrome described by Tanner et al., (1975) as Russell-Silver Syndrome.

1.2.2. Genetics of Russell Silver Syndrome

RSS is a heterogeneous disorder with each case having varying symptomology. The degree of heterogeneity of the syndrome is emphasised by the large number of different potential genetic bases which have been put forward as causal in RSS.

Duncan, Hall, Shapiro & Vibert (1990) reported on four mothers of RSS children who also displayed classical RSS symptoms and this suggested an underlying genetic cause to RSS, with parent to child transmission. No paternal transmission of RSS has been documented; possibly due to maternal bias in data collection, hypogonadism sometimes found in RSS males which has been associated with infertility, or because RSS is only maternally transmitted.

There are reported cases of siblings, but neither of the parents, presenting RSS symptoms (Duncan et al., 1990; Ounap, Reimand, Magi & Bartsch, 2004) and reports of monozygotic twins presenting discordantly with RSS (Samn, Lewis & Blumberg, 1990). These observations suggest that RSS is not a simple parent to child transmission of a genetic abnormality.

Several different specific genes have been proposed as causal in RSS. Children with mutations in chromosomes 8 and 18 have presented with an RSS like phenotype (Christensen & Nielsen, 1978; Schnizel, Robinson, Binkert, Fanconi, 1998), though they have also been found to display additional features, atypical facial dysmorphism and severe learning disabilities, not commonly seen in previously diagnosed cases of RSS. It is suggested that children with mutations of chromosome 8 and 18, do not have true RSS, but a disorder with some overlap with RSS (Hitchins, Stanier, Preece & Moore, 2001). Ring chromosome 15 and deletion of 15q have also been discussed in relation to RSS (Hitchins et al., 2001; Roback et al., 1991; Tamura et al., 1993; Wakeling et al., 1998), however, as with cases described with abnormalities in chromosomes 8 and 18, there were symptoms, microcephaly and severe learning difficulties, not typically seen in RSS (Hitchins et al., 2001).

Maternal UniParental Disomy of chromosome 7 (mUPD7) was for many years the only recognised genetic abnormality in people with RSS (Hitchins et al., 2001; Wakeling et al., 1998) accounting for approximately 10% of all RSS cases (Hannula, Kere, Pirnen, Holmberg & Lipsanen-Nyman, 2001; Hitchins et al., 2001; Kotzot et al., 1995;).

The phenotype of children with RSS and mUPD7 is thought to differ from other RSS cases (Hannula et al, 2001; Preece et al, 1997) with less distinct facial characteristics, less micrognathia and no down-turned corners of the mouth reported (Hannula et al., 2001; Hitchins et al., 2001) but more

severe feeding difficulties, excessive sweating and a more pronounced developmental delay (Hannula et al., 2001).

Recently, a second genetic abnormality has been found which accounts for a further 35% of RSS cases (Eggerman et al., 2006; Schnoerr et al., 2006); an epigenetic mutation of chromosome 11p15. This is one of the most studied clusters of imprinted genes; they control growth and development and children with RSS have been found to have methylation alterations in this domain (Smith, Choufani, Ferreira & Weksberg, 2007). Chromosome 11p15 is also associated with Beckwith-Widemann syndrome (BWS), a disorder characterized by prenatal and postnatal overgrowth. The epigenetic mutation seen in RSS is the opposite to that seen in BWS, with a resulting opposite phenotype (Gicguel et al., 2005; Schonerr et al., 2007). As chromosome 11p15 is a relatively recent finding, no systematic research has assessed for the phenotypical differences of those with RSS-11p15.

With the new knowledge of the 11q15 epigenetic mutation, approximately 45- 50% of cases of RSS can now be confirmed using genetic analysis. The majority of cases, however, still appear sporadically and if there is a genetic cause, this is not yet understood. The heterogeneity of RSS symptom presentation supports several different genetic causes for RSS. It is quite possible that RSS is not one single disorder but several different disorders, all with a clinically similar phenotype, but different underlying causes. Alternatively, all children with RSS may be part of the same disorder, with the genetic differences resulting in different distortions to the same biochemical pathway and therefore similarities in the resulting phenotype (Hitchins et al., 2001, Wakeling et al., 1998). While research in to the genetic basis of RSS is an area of continued interest, in reality the majority of cases are still diagnosed based on symptom presentation. It is therefore important to understand the diagnostic criteria and symptomology of RSS.

1.2.3. Russell Silver Syndrome Diagnostic Criteria

The widely accepted diagnostic criteria for RSS are now, low birth weight (-2SD or below the 3rd centile), continued growth restriction and the presence of characteristic facial features, including a head too large for body, low positioning of facial features and a down-turned mouth; features such as those first described by Russell (1954).

Wollmann et al., (1995) and Price et al., (1999) completed large scale reviews of the incidence of symptoms in children diagnosed with Russell Silver syndrome and found that low birth weight, persistent short stature and phenotypical face shape were reported by Wollmann et al., (1995) in 94%, 99% and 79% of cases respectively. Price et al., (1999) reported slightly lower incidences of these three main features, however their sample size was only a third of that reviewed by Wollmann et al., (1995). Table 1.1 shows a summary of the findings from these two studies.

Table 1.1: Incidence of symptom presentation in RSS, adapted from Hitchins *et al.*, (2001).

Clinical Feature	Wollmann Review incidence N= 143	Price et al incidence, N= 50
Major		
Low birth Weight -1SD	94%	94%
Short stature -1SD	99%	86%
Triangular Face Shape	79%	>62%
Minor		
Clinodactyly V	68%	56%
Relative Macrocephaly	64%	70%
Ear Anomalies	53%	
Skeletal Asymmetry	51%	34%
Brachydactyly V	48%	
Downward turning corners of the mouth	46%	
Muscular Hypertrophy/tonia	45%	
Motor/Neuropsychological delay	37%	38%
Irregular tooth spacing	28%	
Simian Crease	25%	
Squeaky Voice	22%	
Syndactyly	19%	
Café au lait spots	19%	4%
Early or precocious puberty	13%	
Genital Abnormalities		36%
Speech Delay		20%
Camptodactyly		22%
Feeding Difficulties		56%

Additionally to those minor features listed in the table above; blue sclera, late closure of anterior fontanelle, gastrointestinal complications, cardiac conduction defects, arterial septal defects, pulmonary stenosis, renal asymmetry, cystic fibrosis, achromia, hypopigmentation and optic nerve asymmetry have been seen in children with a diagnosis of RSS (Anderson et al., 2002; Christofiridis, Maniadaki & Stanhope, 2005; Patton 1988; Perkins & Hoang-Xuan, 2002; Siegel, Granat & Jones, 1998). Some of these symptoms occur very rarely and may be coincidental rather than as a consequence of RSS

1.2.4. Long term consequences of Russell Silver Syndrome

1.2.4.1. Physical

The gross motor development of children with RSS in early life has been found to be delayed but achieved (Anderson et al., 2002; Donnai et al.; 1989; Patton, 1988; Perkins & Hoang-Xuan, 2002), and this has been attributed to lack of muscle bulk and a relatively large head, making it difficult for the RSS baby to gain head control (Patton, 1988). Studies assessing motor development later in childhood have found that motor and physical development is generally not delayed (Ounap et al., 2004), though those with very low birth weight and marked cranial sparing are at a greater risk of long term motor difficulties (Price et al., 1999). Plotts' (2000) case study of an RSS child and his development into adulthood found that at the age of 20 some fine motor coordination difficulties remained. The paucity of research of RSS children into adolescence and adulthood suggests that long term physical difficulties are minimal.

Speech delays, have been documented in children with RSS, with a significant number of children with RSS receiving speech therapy (Donnai et al., 1989; Lai, Skuse, Stanhope & Hindmarsh, 1994; Price et al., 1999; Saal, Pagon & Pepin, 1985). It can be hypothesised that the speech difficulties are as a consequence of Oro Motor Dysfunction, and are related to the eating difficulties that these children have been found to have (Lai et al., 1994).

1.2.4.2 Cognitive

Silver (1953), in the first reported cases of RSS, suggested that the incidence of learning difficulties may be raised in children with RSS. It has long been believed, however, that in the majority of RSS children, intelligence (Patton, 1988; Price et al., 1999; Tanner et al., 1978) and cognitive ability (Donnai, 1989; Perkins & Hoang-Xuan 2002) are normal with only a subset of children having learning difficulties (Plotts, 2000; Saal et al., 1985). The possibility of motor and speech delays seen in children with RSS, may account, in some cases, for the reported reductions in cognitive ability, with test scores being limited by physical and not cognitive ability (Perkins & Hoang-Xuan, 2002).

Three studies have systematically assessed the cognitive ability and IQ of children with RSS (Lai et al., 1994; Noeker & Wollmann, 2004; Price et al., 1999). Lai et al., (1994) used 8 of the 13

scales of the WISC, the Neale analysis of reading ability and the matching familiar figures test. The data revealed that children with RSS had cognitive abilities that were, on average, 1 SD below that of the general population. Underachievement for reading and mathematics was also found, with girls achieving lower scores than boys, however, there was a male bias in the sample studied. Lai et al., (1994) found that the majority of children reported hypoglycaemia and that IQ scores correlated positively to current head circumference. While birth head circumference and head growth from birth was not found to be significantly related to current WISC IQ, the pattern in the data suggested that this relationship would have reached significance with further data.

The second major study (Noeker & Wollmann, 2004), used the Kaufman Assessment Battery for Children (KAB-C) and found that children with RSS had a mean IQ score significantly below that of an age matched reference population and their siblings. The effect here though was not as strong as that reported by Lai et al., (1994), only a couple of points lower, rather than a full standard deviation. Noeker & Wollmann (2004) found that the RSS group showed markedly lower achievement scores than did control group children, despite only small differences being found for cognitive ability. Unlike Lai et al., (1994), Noeker and Wollmann (2004) did not find that RSS girls achieved lower scores than RSS boys, or that cognitive scores correlated with head growth patterns.

In the third report of cognitive abilities of children with RSS, Price et al., (1999) found that birth length and weight could only account for a small amount of variance in cognitive scores and that there was no correlation between number of hypoglycaemic episodes or feeding difficulties and cognitive scores. The findings of Noeker & Wollmann (2004) and Price et al., (1999), that is, that head growth patterns, number of hypoglycaemic episodes and feeding difficulties, are not correlated with cognitive ability, are at odds with those of Lai et al., (1994). This difference in findings potentially reflects an effect of increased knowledge and treatment of not only the consequences of RSS, such as hypoglycaemia, but also the general improvements in postnatal care for low birth weight babies between the time periods in which the research studies were conducted.

1.2.4.3 Behavioural

The incidence of behavioural problems in children with RSS is an area which has had minimal investigation. Russell (1954) in the first reported cases of RSS, commented on the

hyperactivity seen in the RSS children described, and the subject of Plotts' (2000) case study was reported to experience attention and concentration problems. Lai et al., (1994), however, found that children with RSS did not have apparent poorer attention than did controls. The only piece of published research that exists looking specifically at ADHD incidence in RSS children, is a brief meeting abstract (Bogdanov, Menassepalmer, Lesser, Levy & Marion, 1995). Here 16 children with RSS that had been referred for attentional problems or learning difficulties were investigated. 50% (8) of these cases had a diagnosis of both ADHD and learning difficulties, while 37.5 % reported only learning difficulties, which were usually language based, and 12.5% only had a diagnosis of ADHD. While the sample reported here is small (N=16), the total number of children with an RSS diagnosis is small, making this finding relatively significant. No behavioural problems, other than those that are attention based, have been investigated in RSS.

1.2.5.Hypoglycaemia

Children with RSS are reported to have significant feeding difficulties (Price et al., 1999; Blissett et al., 2001; Anderson et al., 2002; Falkert et al, 2005; Lai et al., 1994; Preece, 1997; Stanhope et al., 1998) and being born SGA and having feeding difficulties is thought to put them at an increased risk of neonatal and childhood hypoglycaemia. Hypoglycaemia is a syndrome which occurs when blood glucose levels drop. Glucose is the principle substrate of the body, including the brain (LaFranchi, 1987; Lteif & Schwenk, 1999; Lucas, Morley & Cole, 1988; Yager, 2002).

1.2.5.1 Neonatal Hypoglycaemia

Neonates are at increased risk of hypoglycaemia, immediately post-natally as they no longer have a maternal nutrient supply and are reliant on glucose from glycogen stores in the liver and muscles, adipose tissue and from nutrients available from food intake. Neonatal hypoglycaemia has been described by one researcher as one of the leading causes of brain injury (Alkalay, Flores-Sarnat, Sarnat, Moser & Simmons, 2005), although other reports say that significant hypoglycaemia leading to neonatal brain injury is rare (Williams, 2005). The rate of neonatal hypoglycaemia in all births has been estimated to be 12.7% (Johnson, 2003), with premature and SGA infants, such as those with RSS, being at the highest risk (Hume, Burchell, Williams & Koh, 2005; Pallotto and Kilbride, 2006), and as many as 44% of children born SGA experiencing neonatal hypoglycaemia (Duvanel, Fawer,

Cotting, Hohlfield & Matthieu, 1999; Hume et al., 2005; LaFranchi 1987; Lteif & Schwenk, 1999; Pallotto and Kilbride, 2006). Infants born SGA as a consequence of intra-uterine growth restriction (IUGR) are at the highest risk of neonatal hypoglycaemia (Johnson 2003), as they have reduced glycogen and adipose tissue stores (Duvanel et al., 1999; Halamek and Stevenson, 1998; Hume et al., 2005; Pallotto & Kilbride, 2006;). Head to arm ratios, which give an indication of adipose tissue, have been found to be the best indicator of hypoglycaemia risk (Johnson et al., 2003). If weight in the neonatal period remains low, as in RSS due to feeding difficulties, there is an increased chance of repeated hypoglycaemic attacks (Duvanel et al., 1999).

Physically, children who have experienced repeated neonatal hypoglycaemic episodes have been found to have smaller head circumferences (6+ hypoglycaemic episodes) (Duvanel et al., 1999) and more neuronal and glial cell damage (Sann, 1990). Hypoglycaemia is not presumed to cause extensive brain damage, but instead specific cell death with some cell types being damage resistant (Alkalay et al., 2005), superficial cortical layers have been reported as most impaired by neonatal hypoglycaemia, especially the optical areas (Filan, Inder, Cameron, Kean & Hunt, 2006; Halamek & Stevenson, 1998; Sann, 1990; Williams, 2005;).

Children who have experienced symptomatic neonatal hypoglycaemia, especially seizures, are known to have a worse neurological outcome than those with asymptomatic hypoglycaemia. This may be because symptoms are only apparent after a prolonged period of hypoglycaemia (Alkalay et al., 2005; Sann, 1990; Yager et al., 2002). Research has found, however, that it is still the number of episodes, rather than the severity which has the biggest impact on children's long term neurological development (Duvanel et al., 1999).

1.2.5.2. Childhood Hypoglycaemia

Children with RSS are reported by parents as having night sweats and other symptoms commonly associated with reduced blood sugar, such as grey pallor and lethargy; although there are few cases of symptomatic hypoglycaemia reported in the literature (Azcona & Stanhope, 2005). Research focussing on the long term cognitive effects of childhood hypoglycaemia is limited, mainly concentrating on those with diabetes and congenital hypopituitarism (Brown et al., 2004) where severe hypoglycaemic episodes are characterised by loss of consciousness and/or seizures. In severe

hypoglycaemia long term cognitive and intellectual consequences have been reported (Ack, Miller & Weil, 1961; Ferguson et al., 2005; Hannonen, Tuploa, Ahonen, Rijkonen, 2003; Hershey, Craft, Bhargava & White, 1997; Rovet & Alvarez, 1997; Ryan, Williams, Finegold & Orchard, 1985;).

The majority of children with diabetes will experience some form of hypoglycaemia, normally asymptomatic or mild, at least once a week (Aman, Karlsson & Wranne, 1989; Barkai, Varnosi & Lukacs, 1998) with some only reporting hypoglycaemia to the degree which is seen in children with RSS. A comparison of children with diabetes with mild hypoglycaemia to those with severe hypoglycaemia, and a control group reported that the severe hypoglycaemia group were receiving more special educational help than either the mild or control groups. However, it was also found that several of the mild hypoglycaemia group were receiving some help (Hannonen et al., 2000)

It has been proposed that the reduced cognitive scores in children with congenital hypopituitarism are due to the early life hypoglycaemia seen in these children (Brown et al., 2004). However, other potential causes for the effects include abnormality in midline brain structures or abnormal growth hormone leading to altered brain growth (Brown et al., 2004).

Brown et al., (2004) highlighted, that although we can look to diabetic research as guidance for the long term effects of hypoglycaemia in other populations, this research is unlikely to reflect exactly what to expect in populations with hypoglycaemia not due to diabetes, in diabetic groups unlike others, no alternative substrate to glucose is available.

1.2.6 Summary of Section

RSS remains a syndrome that is poorly understood. While a proportion of cases can be diagnosed genetically, the significance of the difference in genetic abnormalities remains unclear. The majority of cases of RSS are still diagnosed based on symptom presentation and while there are accepted criteria, diagnosis remains largely subjective.

Early research found that RSS children are cognitively disadvantaged (Lai et al., 1994), however, more recent research suggests that any cognitive deficit is small (Price et al., 1999; Wollmann et al., 1995).

Brain imaging studies have shown that repeated episodes of hypoglycaemia can result in permanent brain injury (Duvanel et al., 1999; Sann, 1990; Alkalay et al., 2005; Filan et al., 2006;

Halamek & Stevenson, 1998; Williams, 2005) and this may be significant when investigating the long term cognitive and behavioural consequences for children with RSS.

1.3. Small for Gestational Age (SGA) and Intra-Uterine Growth Restriction (IUGR)

RSS children are at additional risks due to being small at birth. The long term risks of being born small for gestational age are to be discussed using a systematic review in chapter 3 of this thesis.

The following section introduces the terminology used in low birth weight literature.

1.3.1. Causes of Low Birth Weight

The growth of a foetus is complex with a number of confounding factors which may be impacting on it. Table 1 lists the 4 main types of influential factors with examples.

Table 1.2: Risk factors for low birth weight (Brodsky & Christou, 2004; Fang, 2005).

Confounding Factor	Examples	Consequence for Fetus
Environmental Factors	<ul style="list-style-type: none"> • Socioeconomics • Geographic location 	<ul style="list-style-type: none"> • Impact fetus via maternal factors
Maternal Factors	<ul style="list-style-type: none"> • Mothers stature • Mothers pregnancy weight • Activities undertaken during pregnancy <ul style="list-style-type: none"> ○ Smoking ○ Alcohol consumption ○ Illicit drugs • Maternal malnutrition • Maternal hypertension • Maternal health. 	<ul style="list-style-type: none"> • Affect supply of nutrients and oxygen to fetus.
Placental Factors	<ul style="list-style-type: none"> • Placental abruption • Circumvallate placenta • Umbilical & placental abnormalities 	<ul style="list-style-type: none"> • Available nutrients can not reach fetus as they should.
Fetal Factors	<ul style="list-style-type: none"> • Congenital disorder • Chromosomal genotype • Intrauterine infection 	<ul style="list-style-type: none"> • Fetus unable to use nutrients available to it effectively, not achieving optimum growth.

1.3.2. Differentiating terminology

The birth size of a baby is now known to be important in the long term growth and development for the child. There are different ways to classify low weight babies, it is important that these groups are differentiated as there are likely to be different long term consequences for each group.

1.3.2.1. Low Birth Weight

All neonates weighing less than 2500g at birth are defined as low birth weight babies (Monk & Moore, 2004; Saenger, Czernichow, Hughes & Reiter, 2007). The term 'very low birth weight' has been used in the literature to describe neonates with birth weight <1500g and 'extremely low birth weight' those <1000g. These definitions are arbitrary and do not take into account gestational age, a factor known to independently affect long term development.

1.3.2.2. Small for Gestational Age (SGA)

Historically, a diagnosis of SGA would be made for a baby whose birth weight was below the 10th centile, using standardised growth charts such as Tanner-Whitehouse (1966a,b) or Gardiner-Pearson (1971), when gestational age was taken into account (Wollmann, 1984; Monk and Moore, 2004). For neonates born at term, this weight was 2500g, the same as for low birth weight, however, in premature infants, the 10th centile would be lower, as there had been a shorter period of gestation in which growth could occur. While the 10th centile cut off point has been a standard of practice, it has been suggested that birth weight below the 3rd centile could be used as a better indicator of prognosis (Maulik, 2006; O'Keeffe, O'Callaghan, Williams, Najman & Bor, 2003). The UK90 growth charts (Freeman et al., 1990) have now been found to be more reliable for predicting growth in a normal population (Wright et al., 2002) and the majority of institutions now use these charts, although some have resisted this change (Wright et al., 2002). The centiles used on this chart were calculated using 17 different sets of data collected from across the UK, and account for growth from the age of 23 weeks gestation to 23 years. The charts show 9 centile curves, each two thirds of a SD apart, which allow for improved screening performance and the use of centiles similar to those conventionally used in the Tanner Whitehouse (1966a,b) and Gardiner Pearson (1971) scales. The Department of Health (DoH) recommends that the 2nd and 9th centiles and 91st and 98th centiles are used as clinical cutoffs, therefore, while the 10th centile has been used in past research, the 9th centile used in current charts is likely to be chosen by researchers and clinicians as the cut off point for SGA diagnosis. The World Health Organisation (WHO) have recently suggested the introduction of a new growth chart which takes into account growth dependent on early life feeding, breast or bottle, but these charts are yet to be put into practice.

1.3.2.3. *Intra Uterine Growth Restricted/ Retarded (IUGR)*

Small for Gestational Age and Intra Uterine Growth Restricted, are terms that have historically been used interchangeably however, they do have different meanings (Saenger et al., 2007) and either diagnosis can be present without the other.

SGA is a symptom; this could have been caused by IUGR, while IUGR itself is a diagnosis of a state which could need intervention (Noeker & Wollmann, 2004). A foetus may experience IUGR causing its growth velocity to decrease, but this may not be severe enough for birth weight to fall below the 10th centile and therefore the infant will not be SGA. Equally, a neonate may be born below the 10th centile, but this could be due to factors other than IUGR, such as small maternal size. A neonate will be considered at increased risk when its weight is below the 10th centile, the point at which the infant is also deemed SGA (Maulik, 2006).

Diagnosis of IUGR is difficult and has historically been made postnatally, this may explain the confusion with the term SGA; the two terms were difficult to differentiate. Foetal growth can now be monitored sonographically throughout the pregnancy with particular attention being paid to weight and abdominal circumference. Reductions in the velocity of these measurements are thought to be good indicators of IUGR presence (Maulik, 2006; Fang, 2005). There is evidence, however, that shows that anthropometric measurements at 20 weeks gestation are poor indicators of measurements at 30 weeks gestation and birth (Hindmarsh, Geary, Rodeck, Kingdom & Cole, 2002), suggesting that routine assessment of foetal size in mid to late gestation may be a poor indicator of IUGR presence.

1.3.3 Section Summary

The aim of this section of the literature review was to introduce the terminology which is used in low birth weight literature, highlighting the importance of using the correct literature to understand better the potential consequences to children with RSS. A systematic analysis of the literature with children born SGA has been included in this thesis in study 1.

1.4 Attention Deficit Hyperactivity Disorder

Parents and physicians of children with RSS have anecdotally reported significantly more behavioural problems, and specifically more symptoms of inattention and hyperactivity in RSS children. One of the aims of this research thesis was to investigate the incidence and potential causes of behavioural problems in children with RSS, with an emphasis on hyperactivity/inattention. Hyperactivity/ inattention characterise Attention Deficit Hyperactivity Disorder (ADHD), therefore a literature review of ADHD and its causes and consequences was conducted.

1.4.1. History of ADHD

The history ADHD dates back to the observations of George Still in 1902 who noted a group of children, predominantly boys, showing passionate, defiant, spiteful behaviours and apparent lack of control.

By the 1950s many children were recognised as displaying the behaviours reported by Still and the term ‘minimal brain dysfunction’ had been coined to describe this group of individuals, based on the assumption that all cases of the disorder were caused by defective functioning of specific brain structures. Researchers believed that in many cases the occurrence could somehow be related to a trauma experienced during gestation or birth (Goldstein & Goldstein, 1998).

By the 1970s the term ‘minimal brain dysfunction’ had been replaced with the short lived term ‘hyperkinetic reaction of childhood’ (DSM-II, American Psychiatric Association, 1968). Theories about the cause of the symptoms was also moving away from gestational or birth consequences, following a large scale study which failed to find a consistent association between appgar score (a value calculated for each child at birth based on a number of standard observations) and hyperactivity and inattention development. The stimulant amphetamine had, by this time, been found to be effective in controlling the behaviour of children with the disorder. Ritalin was as a treatment option to reduce the behaviours associated with ADHD, and research was focussing on the systems activated by the stimulant medications to look for a cause of ADHD.

During the 1970s, attention was recognised as a defining feature of the disorder and in the 1980 revision of the DSM (DSM-III, American Psychiatric Association, 1980) it was renamed ‘Attention Deficit Disorder’ this could be diagnosed as ‘with hyperactivity’ or ‘without hyperactivity’.

The revision of the DSM-III in 1987 (DSM-III-R) reverted to a unified description of the disorder named Attention Deficit Hyperactivity Disorder (ADHD) which did not recognise hyperactivity as a differential symptom. The most recent revisions of the DSM, IV (1994) and IV-TR (2000) however, once again acknowledge hyperactivity with three possible diagnoses of ADHD, predominantly hyperactive/impulsive, predominantly inattentive and combined ADHD.

1.4.2 Differentiating ADHD and Hyper Kinetic Disorder

ADHD is the term used by the, DSM-III-R, DSM-IV and DSM-IV-TR (American Psychiatric Association, 1987, 1994, 2000) to describe children and adults with developmentally inappropriate levels of inattention, impulsivity and/or hyperactivity. Hyper Kinetic Disorder (HKD) is the term used by the World Health Organisation's International Classification of Disease-10 (ICD-10, 2007) to describe this same group of individuals. There are subtle differences in the two diagnostic criteria, the ICD-10 is more restrictive and more symptom presentation is needed in order to make a diagnosis of HKD than would be needed for a diagnosis of ADHD (Biderman & Farone, 2005). The ICD-10 criteria are widely used in mainland Europe, while the DSM criteria are predominantly used in the United Kingdom and United States. It has been reported that the incidence of ADHD is greater than that of HKD, and consequently a higher incidence is reported in the UK and USA, than mainland Europe. Extensive epidemiological studies have been carried out worldwide using only the DSM-IV criteria and these have reported that the incidence of ADHD is similar in all countries (for review see Doyle, 2004).

For the purposes of this review ADHD will be used as the main diagnostic term as this is the most widely used term and definition in the literature.

1.4.3. Diagnosing ADHD

The criteria for a diagnosis of ADHD states that some hyperactive or impulsive symptoms must be present before the age of 7 years, the impairment from the symptoms must be seen across at least two settings (e.g. at home and at school) and there must be clear evidence that the behaviours are interfering with their 'developmentally appropriate day to day life' (DSM-IV-TR, American Psychiatric Association, 2000). Before making a diagnosis of ADHD other causes for the behaviours

being elicited must be ruled out, such as frustration, lack of motivation, emotional concerns and other medical conditions.

The DSM-IV-TR (2000) describes three subtypes of ADHD, combined ADHD, predominantly inattentive ADHD, and predominantly hyperactive/impulsive ADHD. To make a diagnosis of combined ADHD, an individual must display at least 6 of the 9 potential symptoms of inattention (see table 1.3) and at least 6 of the 9 potential symptoms of hyperactivity/impulsivity (see table 1.3) set out in the DSM-IV-TR. If the individual only displays 6 of the 9 symptoms of inattention and not of hyperactivity/impulsivity they will be given a diagnosis of predominantly inattentive ADHD and a diagnosis of predominantly hyperactive/impulsive ADHD, will be made when only 6 of the 9 symptoms of hyperactivity/impulsivity are present. Children may initially receive a diagnosis of one subtype of ADHD which could be changed at a later date

Table 1.3: ADHD diagnostic criteria DSM-IV-TR (American Psychiatric Association, 2000)

DSM-IV –TR symptoms of inattention	DSM-IV-TR symptoms of hyperactivity
Often fails to give close attention to details or makes careless mistakes in schoolwork, work, or other activities.	Often fidgets with hands or feet or squirms in seat
Often has difficulty sustaining attention in tasks or play activities.	Often leaves seat in classroom or in other situations in which remaining seated is expected.
Often does not seem to listen when spoken to directly	Often runs about or climbs excessively in situations in which it is inappropriate (in adolescents or adults, may be limited to subjective feelings of restlessness)
Often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace (not due to oppositional behaviour or failure of comprehension.	Often has difficulty playing or engaging in leisure activities quietly.
Often has difficulty organizing tasks and activities.	Often talks excessively
Often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort (such as schoolwork or homework).	Is often ‘on the go’ or often acts as if ‘driven by a motor’
	DSM-IV-TR symptoms of Impulsivity
Often loses thing necessary for tasks or activities at school or at home (e.g. toys, pencils, books, assignments)	Often has difficulty awaiting turn in games or group situations
Is often easily distracted by extraneous stimuli	Often blurts out answers to questions before they have been completed.
Is often forgetful in daily activities.	Often interrupts or intrudes on others, e.g. butts into other children’s games.

1.4.4. Neurobiological basis of ADHD

Kornetsky (1970) was the first to discover that stimulant medication, specifically amphetamines, were an effective treatment for ADHD. These are thought, to operate in the brain by blocking dopamine and nor-epinephrine reuptake and increasing their release. It is thought that they reduce ADHD symptomology by increasing activation of the dopamine and norepinephrine pathways which in turn have an inhibitory effect on the frontal cortical and subcortical structures. Further to the finding of the effects of stimulants and animal models Satterfield & Dawson (1971) suggested that the frontal subcortical circuits were important in ADHD. Matte (1980) highlighted that there were many similarities in the behaviour of adults with frontal lobe dysfunction and children with ADHD.

Based on these findings and further research it is now accepted that ADHD is likely to have its neurological basis in the fronto-subcortical area of the brain, though whether the basis is a lesion in the frontal cortex itself or a region projecting to the frontal cortex remains unclear (Biederman & Spencer, 1999; Faraone & Biederman, 1998).

The advent, and widespread use, of brain imaging techniques would have been expected to reduce the confusion of the area of dysfunction in children with ADHD, however, findings from these retain some ambiguity.

Faraone & Biederman's (2002, in Charney & Nestler) review of structural imaging studies (CT & MRI) assessing for brain abnormalities in ADHD revealed that the majority of studies reported some brain abnormalities, most commonly smaller volumes in the frontal cortex, cerebellum and subcortical structures. The findings were inconsistent, however, which indicates that no one area of the brain routinely different in children with ADHD.

Further to this review Biederman & Faraone (2002, in Charney & Nestler) reviewed ADHD functional imaging studies. As with the structural studies there was a consistent implication of the frontal-subcortical structures, most often frontal-striatal-pallidial-thalamic circuit which is involved in feedback to the cortex to regulate behaviour. As with the structural studies though these findings were trends and not definitive.

Neuro-imaging studies have shown that, in inhibition tasks, children with ADHD activate areas in the posterior of the brain which were not active in controls on the same task (Durstun et al.,

2003) suggesting the use of alternate strategies by children with ADHD, due to a frontal-subcortical area dysfunction.

In summary, dysfunction in the frontal-subcortical structures is implicated in ADHD, both from neuropsychological and structural and functional brain scanning studies. The actual location of the damage remains ambiguous and this potentially reflects several different damaged areas in ADHD.

1.4.5. Causes of ADHD symptomology

An executive dysfunction has been proposed as the underlying difficulty in individuals with ADHD. Executive Functions (EFs) are self regulatory neurocognitive processes that include the ability to inhibit, shift set, plan, organize, use working memory, problem solve and to maintain a set in order to attain future goals (Willcutt, Doyle, Nigg, Faraone & Pennington, 2005; Seidman, 2006). Individuals need to utilise EFs in order to successfully complete novel tasks which require flexibility and adaptation. The brain areas thought to be responsible for executive functions are in the frontal area, specifically the orbitofrontal cortex which is important in regulating and controlling emotions, dorsolateral prefrontal cortex, which is specialised in organising and integrating incoming information and acts as a memory buffer, and the medial area which is important in preparation and direction of learned complex movements. As the frontal-subcortical circuit have been implicated in ADHD in structural and neuroimaging studies (Biederman & Faraone, 2002, in Charney & Nestler), executive dysfunction, which also has a frontal association seems a logical area to assess further. It has been suggested that individuals with ADHD may have difficulties in a specific EF domain, or general difficulties (Willcutt et al., 2005).

Barkley (1997) proposed a unified theory of ADHD, hypothesising that the main problem in individuals with ADHD was one of inhibitory control and, as a consequence of inhibitory control deficits, other executive controls strategies were compromised (Seidman, 2006). Barkley's (1997) theory has been investigated but a review of the research would go beyond the scope of this literature review. Three large scale meta-analyses which have been carried out on the available research in recent years (Willcutt et al., 2005; Castellanos et al., 2006; Nigg et al., 2005). The meta-analyses all reported that children with ADHD and controls were found to differ across all EF domains, with most

difficulties detected in the stop-signal task; this task is thought to rely on inhibitory control. Sampling procedure, ADHD diagnostic criteria, intelligence, reading ability and other co-morbid disorders could be excluded as confounders for the deficient functioning in EF tasks (Willcutt et al., 2005). While initial findings appear to support the hypothesis of Barkley (1997), all three of the meta-analyses concluded, however, that in a larger than expected proportion of children with a diagnosis of ADHD, no EF deficit was detected. EF alone is not sufficient to account for all cases of ADHD (Castellanos et al., 2006; Nigg et al., 2005; Willcutt et al., 2005).

A second, less investigated theory, suggested that the underlying mechanism of ADHD is delay aversion (Sagvolden, Aase, Zeiner & Berger 1998). It was hypothesised that individuals with ADHD have a neurobiologic impairment in the control of the ratio of present action to future reward. The overall outcome of this is that individuals with ADHD are averse to any delay. When the individual can reduce the delay they will, when they cannot they will make diversions to make the delay feel shorter (Sounuga-Barke, 2005). These actions result in the behavioural deficits seen in those with ADHD. Performance in tasks which assess delay aversion, most commonly delay-reward tasks, has been found to correlate with the incidence of ADHD (Solanto et al., 2001).

Both delay aversion and inhibitory control have been found to be significantly related to ADHD (Castellanos et al., 2006; Solanto et al., 2001), however, they have not been found to correlate to one another (Solanto et al., 2001) suggesting that ADHD is a multifactorial disorder (Nigg et al., 2005; Sounuga-Barke, 2005; Castellanos et al., 2006).

It was suggested, even prior to the acceptance that executive dysfunction cannot fully account for ADHD, that ADHD is actually two separate disorders, the first being what is known as predominantly inattentive ADHD (ADHD-IA) and the second predominantly hyperactive/impulsive ADHD and combined ADHD (ADHD-C) (Hill, 1998; Milich, Balentine & Lynham, 2001; Baeyens, Roeyer & Walle, 2006). Milich et al., (2001) summarised that 'ADHD-C and ADHD-IA are distinct and unrelated disorders with no defining features in common, with each disorder having a completely different personality'.

Individuals with a diagnosis of ADHD-IA have been described as rather dreamy, inert (Sagvolden, Johansen, Aase & Russell, 2005), easily confused, hypoactive, daydreamers (Barkley,

2001) with a sluggish cognitive tempo (Baeyens et al., 2006). The inattention problems seen in individuals with inattentive ADHD, are difficulties in selective or focused attention and a slow tempo of information processing (Murphy Barkley & Bush, 2002; Barkley, 1997; Barkley, 2001).

Individuals with predominantly hyperactive/impulsive ADHD and combined ADHD however, are described as distracted and as having reduced persistence (Sagvolden et al., 2005) with difficulties in response inhibition, persistence of attention and resistance to distraction (Murphy et al., 2002; Barkley, 1997).

At a neuroanatomical level no differences have been found between children and adults with different ADHD subtypes, and at a neurophysiological level any differences found have generally been quantitative, the same areas are affected but to differing degrees (Baeyens et al., 2006). This lack of difference, between the two diagnosis, may indicate that the two subtypes should remain part of one larger disorder, however, research is still lacking in this area and these findings are based on a few small scale studies. Further research may dispute what is currently accepted.

In summary, the underlying cause of ADHD remains unclear, while inhibitory control and delay aversion have been found to be deficient in individuals with ADHD, they are not found to be correlated, suggesting that ADHD is a multi-factorial disorder. In addition, ADHD-IA and ADHD-C cannot currently be differentiated neuroanatomically or neurophysiologically, despite very different personality presentations. Once a complete understanding of those with ADHD-C has been obtained, this may make it easier to differentiate these two disorders.

1.4.6. Diagnosing ADHD

The diagnosis of ADHD remains clinical, no medical test has been found that will clearly ascertain whether or not a child has ADHD (Biederman & Faraone, 2005, Hill, 1998, Swanson, Sergeant, Taylor, Sonuga-Barke, Jensen & Cantwell, 1998), this reflects a lack of consensus regarding the underlying difficulty and potential heterogeneity of ADHD. Despite the potential for subjectivity, diagnosis of ADHD has been found to be reliable, with trained professionals consistently agreeing on its presence or absence (Biederman & Faraone, 2005; Farone, Biederman & Zimmerman, 2005). Questionnaires are widely used within epidemiological studies to ascertain the incidence of ADHD and have displayed excellent convergence between scores and ADHD diagnosis (Biederman et al.,

1993). Questionnaires, however, may over report the incidence of ADHD (Szatmari, Orford & Boyles, 1989). Use of questionnaires in clinical diagnosis should be approached with caution and reaffirmed using interview methods of assessment (Swanson et al., 1998).

1.4.7. ADHD Incidence

There are huge discrepancies in the reported incidence of ADHD, with estimates ranging from 5% to 16% of the school age population (Faraone, Monuteaux, Biederman, Cohan & Mick, 2003; Biederman & Farone, 2005; Wolarich, Hannah, Baumgaertel & Ferurer 1998). Clinical data has been found to report a higher incidence of ADHD-C than ADHD-IA (55%:27%) (Lahey et al., 1994), while population studies have found that ADHD-IA is the most prevalent of the ADHD subtypes (Faraone, Biederman, Weber & Russell, 1998; Gaub & Carlson, 1997). This finding is most likely due to sampling bias of clinical data; children with ADHD-IA are much less likely to cause the level of concern in parents, due to fewer externalising behaviours, which might result in a referral (Sagvolden et al., 2005).

The ratio of ADHD in males to females is estimated to be between 3:1 and 9:1 (Swanson et al., 1998; Milich et al., 2001) for both combined and predominantly hyperactive ADHD. Predominantly inattentive ADHD incidence however, is estimated to be closer to 1:1 (Swanson et al., 1998; Milich et al., 2001), possibly due to the subtler symptomology. The male to female ratio for ADHD as a whole, has been found to be greater in clinical than community studies, possibly reflecting the higher rate of referral for males. ADHD is known to be more disruptive in males than females, boys having a higher reported rate of hyperactive, impulsive, conduct and oppositional problems (Swanson et al., 1998; Biederman & Farone, 2005; Biederman, 2005).

1.4.8. Cause of ADHD

There has been a great deal of research looking at the causes of ADHD. Despite this the cause and mechanism of the disorder remains poorly understood.

1.4.8.1 Genetics

Familial research has found that parents of children with ADHD have a 2-8 fold increased risk of having ADHD themselves (Faraone & Biederman, 1998; Millichap, 2008) and the majority of children with ADHD will have a first or second degree relative with ADHD and/or learning

difficulties (Millichap, 2008). Adoption studies have found that adoptive families are less likely to display ADHD or related disorders than do biological relatives (Cantwell, 1975; Morrison & Stewart, 1973). While genes are known to play an important role in ADHD, there is also expected to be an effect of environment, 79% of monozygotic twins have been found to be concordantly diagnosed with ADHD, while only 32% of dizygotic twins were found to be. If ADHD had a purely a genetic cause, monozygotic twins would be expected to have 100% concordance.

It is suggested (Biederman & Faraone, 1998), that several genes are implicated in ADHD, all having a modest effect. This would account for the high population prevalence, high concordance in monozygotic twins but only modest effects in first degree relatives.

1.4.8.2 Environmental

No one environmental risk factor for ADHD has been found, though several have been suggested.

Lead exposure and contamination has been found to lead to ADHD-like behaviours (Gittelman & Eskenazi, 1983; Braun, Kahn, Froehlich, Auinger & Lanphear, 2006; Nigg et al., 1998). This, however, is almost certainly not the cause of ADHD in the majority of cases, where on many occasions ADHD is present without lead exposure.

Events and complications during pregnancy and birth, such as toxæmia, maternal bleeding, fetal distress and prolonged labour, have been found to be associated with an increased incidence of ADHD (Faraone & Biederman, 1998; Milberger, Biederman, Faraone, Guite & Tsuang, 1997; Sprich-Buckminster, Biederman, Milberger, Faraone Lehman, 1993). Events that result in reduced oxygen supply to the fetus/neonate for a prolonged period are more likely to be associated with increased ADHD incidence than acute traumatic events (Faraone and Biederman, 1998; Biederman & Faraone, 2005). Fetal distress due to environmental factors may selectively damage striatal neurons and affect the developing frontal lobe basal ganglia neural network (Swanson et al., 1998).

Birth weight is an important factor in parental reports of attentional problems, with lower birth weight infants experiencing more inattention (Hack et al., 2004, Indredavik, Vik, Heyerdahl, Kulseng & Brubakk, 2005; O'Keeffe, O'Callaghan, Williams, Najman & Bor, 2003; Mick, Biederman, Faraone, Guite & Tsang, 2002b; Elgen, Lundervold, & Sommerfelt, 2004) and

hyperactivity (Kelly, Nazroo, McMunn, Boreham & Marmot, 2001). Reductions in other birth measurements e.g. ponderal index, head circumference to length ratio, and head circumference alone (Lahti et al., 2006; Wiles, Peters, Heron, Gunnell, Emond & Lewis, 2006), have also been reported to be significantly linked to increased attention problems. In combination these findings offer strong support for an association between reduced prenatal growth and increased attention difficulties.

The degree of birth weight compromise has been found, by some researchers, to be a significant factor when assessing the long term affects on attention (Linnet et al., 2006; O'Keeffe et al., 2003). Linnet et al., (2006) found that there was a two fold increase in parental reports of attention problems in those born below 2000g, and only a 70% increase in those born between 2000g -2500g, in comparison to those with birth weight greater than 3000g. Other researchers however, have reported that extent of birth weight compromise is not important when reporting attentional difficulties (Elgen et al., 2004; Breslau, 1995). Elgen et al., (2004) found that degree of low birth weight was not associated with increased difficulties on tasks which assess attention; those born below 1500g were found to perform comparably to those born 1500g -2000g. It is possible that at the lower end of the birth weight scale there is a ceiling effect of attention difficulties, possibly at 2000g, as Elgen et al., (2004) only studied groups up to this weight, while Linnet et al., (2006) and O'Keeffe et al., (2003) worked with children with higher birth weights.

It is important in LBW research, as already discussed in section 1.3, to differentiate according to the cause of LBW. Those born SGA and LBW are likely to have a low weight due to compromised growth in-utero. Those born LBW due to prematurity are less likely to have compromised growth in-utero, with a low birth weight which is appropriate for their gestational age. Premature children will face additional complications, independent of their low birth weight, therefore findings with groups which do not differentiate or control for prematurity, will be heterogenous and it will be difficult to make cause attributions. The small body of research which controls for gestational status will now be discussed.

Robson & Cline (1998) found that children born SGA, without additional complications, displayed no more impulsivity or inattention than a control group, while those born SGA, with additional neonatal illness, were found to display significantly more inattention than controls (Robson

& Cline., 1998). As a general cognitive deficit was not reported in any of the groups assessed by Robson & Cline (1998) any differential findings were attributed to an attention difficulty.

Indredavik et al., (2005) directly compared parental reports of children born LBW with those born SGA. The LBW group reported significantly more symptoms of inattention and greater levels, approaching significance, of symptoms of hyperactivity than those born SGA. Importantly here, the SGA group were not found to differ from controls for inattention or hyperactivity. Indredavik et al., (2005) followed up the parental reports with MRI scans which showed that those with LBW and ADHD had a thinning of the corpus callosum and white matter reduction, however, those in the SGA group who had a diagnosis of ADHD were better explained by socioeconomic factors. These conclusions were mirrored by Robson & Cline (1998) who commented that 'IUGR risk appears to increase a child's environmental vulnerability'. Mick et al., (2002b) found that LBW was a significant risk factor for ADHD and this could not be accounted for by parental ADHD, parental antisocial behaviour, maternal substance abuse or social class, and therefore LBW alone does account for a relatively small number of cases of ADHD.

1.4.8.3. ADHD and maternal smoking

Maternal smoking during pregnancy has been consistently found to be associated with an increased incidence of ADHD (Mick, Biederman, Faraone, Sayer & Kleinman, 2002a; Milberger, Biederman, Faraone & Jones, 1998; Thapar et al., 2003; Button, Maughan & McGuffin, 2007 (for review), Linnet et al., 2003 (for review)) with children of smokers found to be an estimated three times more likely to receive a diagnosis of ADHD than children of non-smokers (Linnet et al., 2003). This significant effect has been found to exist even when other factors known to be associated with offspring ADHD development, e.g. socioeconomic status, maternal IQ and parental ADHD (Hill, 2002) are controlled (Milberger et al., 1998; Linnet et al., 2005). It is hypothesised, from animal research findings, that smoking results in a number of changes in the brain of the developing foetus and this is the mechanism causing an increased incidence of ADHD (Button et al., 2007).

It is important to note that maternal smoking is also associated with low birth weight, however, Mick et al., (2002a) found that there is a subset of low birth weight infants whose ADHD incidence cannot be accounted for by maternal smoking.

1.4.3.8.4 Psychosocial factors

There is research to suggest that psychosocial factors are important in ADHD causality. Children with ADHD were more likely to live in a home with marital distress, single parenthood, family dysfunction, low maternal education and low social class (Offord et al., 1992; Barkley, 1990). It has already been shown that there is a moderate familial link in ADHD (Faraone & Biederman, 1998; Milichap, 2008), therefore there is a probability that parents of children with ADHD will also have ADHD or ADHD like symptoms. People with a diagnosis of ADHD may have difficulties with education and relationships (to be discussed further below). Therefore, the effects found by Offord et al., (1992) and Barkley (1990) may represent the home environment of a parent with ADHD and, as shown, there is a good probability their child will also show ADHD symptoms. The ADHD experienced by the parents might cause a less than optimal home life AND the child is likely to also have ADHD due to heritability.

1.4.3.8.5. Summary of causes of ADHD

In summary, the cause of ADHD remains poorly understood. There does appear to be a strong genetic component, but environment, especially pre- and post- natal complications and low birth weight have also been found to play a role. It is likely that ADHD has multiple etiologies (Biederman & Spencer, 1999; Faraone & Biederman, 1998), in some sufferers there may be a single genetic cause (Biederman & Spencer, 1999), while in others it may be purely environmental and, in addition, there may be some who have ADHD who have a genetic propensity which is activated by an environmental cause and this interaction has increasingly been recognised as important (Millichap, 2008).

1.4.9. Long term consequences of ADHD

1.4.9.1. Adulthood

It has been reported that between 4% and 75% of individuals diagnosed with ADHD in childhood, will continue to display ADHD symptoms into adulthood (Corbett & Stanczak, 1999; Hervey, Epstein & Curry, 2004); source of symptom reporting is thought to be responsible for this huge variation (Hervey et al., 2004). Hyperactive symptoms are known to diminish to a greater extent than inattentive symptoms as the individual enters adulthood (Faraone, Biederman, Spencer, Wilens, Siedman, Mick & Doyle, 2000) and the male bias in presentation is thought to be less pronounced in

adults than in children (Faraone et al., 2000). It appears that there is a high familial loading of adult ADHD, with a larger genetic role in persistent than remitting ADHD (Faraone et al., 2000).

1.4.9.2. Childhood

Whatever the cause of ADHD there are associated long term difficulties that all the children, and adults, may face. Children with ADHD are known to be at great risk socially and have many difficulties in forming relationships (Holowenko, 1999). They are not as often chosen as partners in play etc, due to being socially inept and this could lead to low self esteem, poor peer relationships and parental conflict (Biederman, 2005). Emotional problems seen in children with ADHD are most likely a consequence of their inability to form relationships, rather than a consequence of ADHD itself.

Research has found that, in samples of children with ADHD, between 45 – 94% have a diagnosis of a concurrent behavioural disorder such as oppositional defiant disorder, conduct disorder or an anxiety disorder, and additional difficulties have been found to be at the highest rate in children with combined ADHD (Murphy et al., 2002, Sergeant, Geurts & Oosterlaan 2002; Kessler, 2004; Barkley, Fischer, Smallish & Fletcher, 2004).

In addition to behavioural difficulties, 20 – 40 % of children with ADHD are thought to have at least one type of learning difficulty in reading, spelling or maths (Murphy et al., 2002). This finding may not be entirely true and may merely reflect the fact that children with ADHD may have difficulties retaining attention in situations where these skills are being tested (O'Regan, 2005). Specific learning difficulties such as dyslexia, dyspraxia and dyscalculia, are thought to be seen in approximately 40% of children with a diagnosis of ADHD. There may additionally be an impairment in completing standardised testing, and in combination with maintaining attention in classroom situations, be putting them at high risk of academic failure (Biederman, 2005). Academic failure has been found to be a more significant problem in children with predominantly hyperactive/impulsive and combined ADHD (Murphy et al., 2002) than in those with predominantly inattentive ADHD. In the long term, childhood ADHD has been associated with increased delinquency, peer rejection, externalising antisocial disorders, smoking and substance abuse (Biederman, 2005; Murphy et al., 2002).

1.4.10 Summary of Section

ADHD is thought to have a neurobiological basis in the fronto-subcortical circuits though the exact location of dysfunction remains unclear. The underlying dysfunction also remains ambiguous, although an executive dysfunction is likely in at least a proportion of diagnosed cases of ADHD, with delay aversion potentially accounting for further cases. Diagnosis of ADHD is largely subjective, though has been proven reliable, and the incidence of ADHD is reported to be between 5-16% of school age children. Males have been found more often to receive a diagnosis of ADHD, however, when little emphasis is put on externalising symptoms the male to female ratio is closer to 1:1.

There is a strong argument for the role of genetics in ADHD although this cannot account for all incidences, with environmental factors including lead poisoning and post-natal and birth complications being cited. Those born small for gestational age, at term, as is the case in RSS, have been found to report significantly more symptoms of ADHD only when there were additional post natal complications.

It is important to detect ADHD symptoms as early as possible as there are many potential negative consequences for the the child with ADHD.

1.5 Autistic Spectrum Disorder

As with ADHD, parents and physicians of children with RSS have anecdotally reported an increased incidence of Autistic Spectrum Disorder (ASD). An aim of this thesis is to assess the incidence of ASD in an RSS population and to look for potential causes if a raised incidence is detected. In order to understand ASD better this literature review assesses the history, diagnostic criteria and reviews potential causes and consequences of ASD.

1.5.1 History of ASD

Kanner (1943) was one of the first researchers to report the behaviours in children which are now known to be central to a diagnosis of ASD, these included difficulties with reciprocal social interaction, communication and ritualistic and stereotyped routines. It was recognised that despite the children displaying profound social deficits, they could relate to objects in a purposeful and intelligent way (Kanner, 1946) and while the children described by Kanner (1943) displayed a significant disturbance in cognition, this was in the absence of an obvious physical or brain dysmorphology.

In 1944, Austrian Hans Asperger reported a group of children with similar behaviours to those described by Kanner (1943), but with less intellectual impairments. Due to the political climate at the time, World War II, Asperger's research remained less widely distributed than that of the American, Kanner.

Kanner first recognised an autistic syndrome in 1943, but it was not included in the original release of the DSM-I (1952) or its first revision (DSM-II, 1968). Those with autistic like symptoms were at this time, diagnosed as “schizophrenic reaction, childhood type”.

The DSM-III (1980) was the first to recognise autism as a disorder, though different sub-types were not included and “infantile autism” was used to describe all children in the diagnostic bracket. The DSM-III-R (1987), retained the diagnostic criteria for autism of the DSM-III (1980), but removed “infantile” from the diagnosis.

Wing and Gould's (1979) large scale epidemiological study noted a distinct group of children with the triad of impairments described by Kanner (1943) but they further reported that children displayed varying degrees of the triad of impairments and were the first researchers to propose the concept of an autistic spectrum of disorders..

In 1981, Lorna Wing brought the work of Asperger to the greater attention of many researchers, with the purpose of demonstrating that autism could occur in individuals with well developed language and cognitive skills, at odds with previous beliefs. Asperger's syndrome was coined to describe the group of children at the more cognitively able end of the autistic spectrum and was recognised with separate diagnostic criteria by the DSM-IV (1998) and DSM-IV-TR (2000).

1.5.2. Diagnosing ASD

The most recent updates of the DSM (DSM-IV, 1998; DSM-IV-R, 2000) describe a group of ‘pervasive developmental disorders’, which recognise Autistic Disorder (AD), Aspergers Syndrome (AS), and Pervasive Developmental Disorder- Not Otherwise Specified (PDD-NOS), all coming under the umbrella of Autistic Spectrum Disorders (ASD). In addition Retts syndrome and childhood disintegrative disorder are included as pervasive developmental disorders, though these are not seen as part of the autistic spectrum. The DSM-IV and DSM-IV-R list a possible 16 symptoms (see table 1.4) that may be seen in children with AD. To receive a diagnosis of AD a child must demonstrate at least

six of these, with at least two qualitative impairments in social interaction (column 1), and one qualitative impairment in communication (column 2) and one restricted, repetitive and stereotyped pattern of behaviour, interests and activities (column 3).

Table 1.4: Autistic Disorder (AD) diagnostic criteria DSM-IV-TR (American Psychiatric Association, 2000)
A child must display at least 6 of the listed behaviours with at least 2 behaviours from column 1 and one each from column 2 and 3 to receive a diagnosis of AD.

	1	2	3
	Qualitative impairment in social interaction	Qualitative impairment in communication	Restricted, repetitive and stereotyped patterns of behaviour, interests and activities
A	Marked impairment in use of multiple nonverbal behaviours such as eye to eye gaze, facial expression, body postures, and gestures to regulate social interaction	Delay in, or 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)	Encompassing preoccupation with one or more stereotyped and restricted patterns of interest that is abnormal either in intensity or focus
B	Failure to develop peer relationships appropriate to developmental level.	In individuals with adequate speech, marked impairment in the ability to initiate or sustain a conversation with others.	Apparently inflexible adherence to specific, non-functional routines or rituals
C	A lack of spontaneous seeking to share enjoyment, interests, or achievements with other people (e.g. by lack of showing, bringing, or pointing out objects of interest).	Stereotyped and repetitive use of language or idiosyncratic language.	Stereotyped and repetitive motor mannerisms (e.g. hand or finger flapping or twisting, or complex whole body movements).
D	Lack of social or emotional reciprocity	Lack of varied, spontaneous make-believe play or social imitative play appropriate to developmental level	Persistent preoccupation with parts of objects.

The diagnostic criteria for AS, taken from the DSM-IV-TR (2000), can be seen in table 1.5. As with a diagnosis of AD, at least two symptoms of qualitative impairment in social interaction must be apparent, along with at least one symptom of restricted repetitive and stereotyped pattern of behaviour, interest and activities. In addition, in order to receive a diagnosis of AS, and not AD, the DSM-IV-TR states that the disturbance must cause clinically significant impairment in social, occupations or other important areas of functioning, there must not be a significant delay in language, cognition or age appropriate self-help skills and children must not meet criteria for any other specific pervasive developmental disorder or schizophrenia.

Table 1.5: Asperger’s Syndrome diagnostic criteria DSM-IV-TR (American Psychiatric Association, 2000). A child must display at least two symptoms from column 1 and one from column 2, with no communication difficulties, to receive a diagnosis of AS.

	A	B
	Qualitative impairment in social interaction	Restricted, repetitive and stereotyped patterns of behaviour, interests and activities
1	Marked impairment in use of multiple nonverbal behaviours such as eye to eye gaze, facial expression, body postures, and gestures to regulate social interaction	Encompassing preoccupation with one or more stereotyped and restricted patterns of interest that is abnormal either in intensity or focus
2	Failure to develop peer relationships appropriate to developmental level.	Apparently inflexible adherence to specific, non-functional routines or rituals
3	A lack of spontaneous seeking to share enjoyment, interests, or achievements with other people (e.g. by lack of showing, bringing, or pointing out objects of interest).	Stereotyped and repetitive motor mannerisms (e.g. hand or finger flapping or twisting, or complex whole body movements).
4	Lack of social or emotional reciprocity	Persistent preoccupation with parts of objects.

PDD-NOS, the third diagnosis possible in the autistic spectrum in the DSM-IV-TR (2000), is made when a child displays some of the symptoms seen in pervasive developmental disorders but insufficient to receive a diagnosis of either AD or AS.

The diagnostic criteria set out by the DSM-IV-R (2000) for AD and AS are based on clinical observations which raises the question of the validity of two separate diagnoses. The basic distinction between AS and AD, according to the DSM, is that those with a diagnosis of AS will not have reduced cognitive ability or delayed speech. A diagnosis of High Functioning Autistic Disorder (HFAD) however can be made if the person has delayed speech but is of normal intelligence (IQ = 70+). Language ability is therefore key to differentiating those with a diagnosis of AD from those with a diagnosis of AS.

It has been shown that those with a diagnosis of AS do not display language delays but the validity of AS as unique and separate from AD is lacking (Macintosh & Dissanayke, 2004; Frith, 2004, Cuccaro et al., 2007; Howlin, 2003). Both AS and AD are heterogenous diagnoses which overlap and form part of the greater Autistic Spectrum of Disorders (Frith, 2004). Many children with AS have demonstrated, following a diagnosis based on lack of language delay, difficulties in comprehension, vocabulary, and the social use of language (Howlin, 2003). If the diagnostic criteria

were followed strictly these children should have a diagnosis of HFAD, and not AS, and in fact very few would ever receive a diagnosis of AS (Howlin, 2003).

By simply using the criteria and definitions set out by the American Psychiatric Association the wide variability within not only the autistic spectrum, but also within each individual diagnosis i.e. AD or AS, cannot be seen (Johnson & Myers, 2007) and there are potentially further subtypes in the autistic spectrum which are not currently recognised. Outside the main autistic spectrum there is believed to be a 'broader phenotype' where individuals would not meet criteria for diagnosis on the autistic spectrum, but display mild symptoms. It is estimated that this phenotype occurs in 1 in 5 first degree relatives of children with ASD (Rutter, 2005) with higher rates of mild impairments found in parents and, to a lesser extent, siblings of those with an ASD diagnosis, than in controls (Bailey et al., 1998).

As there is currently little evidence to differentiate AS and AD empirically, the term ASD is often used to describe all those on the autistic spectrum and research tends to focus on causes and consequences for those on the spectrum as a whole, rather than focussing on individual diagnoses.

1.5.3. Incidence of Autistic Spectrum Disorder

The reported incidence and prevalence of ASD has been found to have increased dramatically in recent years (Fombonne, 1999; Powell et al., 2000; Wing & Potter, 2002). Early reports of the incidence of ASD were quite conservative, 4.3-4.5 in every 10,000 children (Lotter, 1966; Brask, 1970) but recent estimates place this figure much higher. Powell et al., (2000) reported 16.2 in 10,000 children have a diagnosis of AD and while Chakrabati et al., (2001) reported comparable rates for the incidence of AD, they also reported a rate of 45.8 in 10,000 for the entire autistic spectrum. The relatively recent estimates, of Rutter (2005) and Fombonne et al., (1999), are that between 30 and 60 children in every 10,000 will receive a diagnosis of an ASD. The large scale research of the centre for disease control and prevention in the United States, conducted in 2007, gives the most recent estimates of ASD incidence, with 34 in every 10,000 children having a diagnosis of AD and 67 in every 10,000 a diagnosis of ASD.

While the increasing reported incidence of ASD may reflect a true increase in the occurrence of ASD it could also be due to changes in diagnostic criteria, different study methods being used over

the years, the increasing awareness of autism and the spectrum and the recognition that ASD can be associated with other conditions (Wing & Potter, 2002).

1.5.4 Neurobiological basis of ASD

As ASD is heterogenous in symptom presentation, the underlying neurological dysfunction is also heterogenous with no consistent change detected in the autistic brain. It is possible that all cases of ASD have a common neural basis or, alternatively, different brain systems are affected but with similar core deficits (Lord et al., 2000).

One of the most observed differences in the brains of children with ASD is a larger than expected head size and brain volume (Lord et al., 2000; Bailey et al., 1998; Minshaw & Williams, 2007). Dysfunction, detected using post mortem and imaging studies, has been found in the cerebellum, limbic system, frontal and temporal cortexes, corpus callosum and basal ganglia (Paya-gonzalez & Fuentes-Menchaca, 2007; Lord et al., 2000; Brambilla et al., 2003; Schumann et al., 2004) and loss of the purkinje cells in the cerebellum of those with ASD has often been reported (Bailey et al., 1998; Kemper & Baumen, 1998).

As social disturbance is the main behavioural symptom of ASD, assessment of the brain areas involved in social performance in controls is thought to give an indication of the brain areas which may be dysfunctional in those with ASD. Social behaviours have not been found to be limited to one brain area, it is however known that the amygdala plays an important role (Baron-Cohen et al., 1999; Lord et al., 2000) and in the macaque monkey an apparent autistic syndrome has been observed, following an amygdalotomy (Bachevalier, 1996).

1.5.5. Cause of Autistic Spectrum Disorder

1.5.5.1. Genetics

Initially it was doubted that ASD was heritable, as there was no clear parent child link and sibling incidence was found to be low (Hanson & Gottesman, 1976). However more recent research supports a strong genetic component to ASD, with genetics currently being the best established risk factor (Rutter, 2005). ASD is now thought to be the most heritable of all multi-factorial childhood psychiatric disorders (Rutter, 2005).

Familial studies have been found to support a genetic component to ASD. Monozygotic twin concordance is thought to be between 60-90%, while dizygotic twin concordance is much lower, 5-10% (Rutter, 2005; Bailey et al., 1995), for AD only with twin concordance for the whole autistic spectrum of disorders thought to be much higher (Spence, 2004). ASD has been shown to have sibling concurrence of between 2-6% while the risk of a younger sibling of a child without ASD developing ASD was found to be <0.5% (Spence, 2004). The risk of a child being diagnosed with ASD, following a sibling diagnosis, has been reported to be as high as a 25 fold increase over the general population prevalence (Zhao et al., 2007).

Siblings and parents of an affected child are more likely than controls to show subtle cognitive or behavioural features that are qualitatively similar to those seen in children with ASD (Bolton et al., 1994; Bishop et al., 2004; Glasson et al., 2004). This suggests that more than one gene is involved in the development of ASD (Glasson et al., 2004; Gupta & State, 2007), with estimates ranging from 5-15 contributing genetic loci or regions (Risch et al., 1999; Rutter, 2005).

Approximately 10% of cases of ASD are associated with a genetically identifiable disease or disorder (Rutter, 2005; Johnson & Myers, 2007; Muhle et al., 2004; Abrahams & Geschwind, 2008), including Tuberous Sclerosis (TSC), Prada-Willi/Angelmann syndrome, fragile X and neurofibromatosis (Newschaffer et al., 2002; Muhle et al., 2004; Spence, 2004).

Approximately 1-3% of children diagnosed with ASD are thought to have TSC (Smalley, 1998) and this is approximately 25% of all those with a TSC diagnosis (Muhle et al., 2004). In the case of TSC, it is thought that the link between ASD and the disorder is not genetic, but instead a result of the brain damage associated with the tubers and seizures commonly seen in TSC (Wiznitzer, 2004).

There is a male bias in the incidence of ASD which suggests involvement of a mutation of the X chromosome, though this has yet to be found. There is currently no identifiable genetic lesion which results in the normal physiognomy seen in children with ASD and is found predominantly in males (Rutter, 2005).

Although many different genes and proteins have been implicated in ASD, few significant genetic linkages have been found (Muhle et al., 2004), as it is expected that ASD is the result of genes acting synergistically, it may be some years before a complete genetic picture of ASD is formed.

1.5.5.2. Non-heritable factors

An increased prevalence of ASD has been reported over the last decade (Newschaffer et al., 2002; Fombonne et al., 1999; Powell et al., 2000; Wing & Potter, 2002) and it is suggested that non-heritable risk factors for ASD are playing a role in a large number of cases (Rutter, 2005).

Pre- and peri-natal risk factors for ASD have been investigated for many years, and with the reported increased prevalence of ASD in the last decade research has increased. It is possible that pregnancy, delivery and neonatal complications are acting through an independent pathway from genetic ASD, or that there is an interaction, with an increased genetic disposition being exacerbated by an insult at a critical time in the developmental process (Hultman et al., 2002).

Early studies, investigating pre- and peri-natal risk factors, tended to have small sample sizes, use clinical groups rather than being epidemiological research and use a single suboptimal obstetric conditions score which ignores the fact that different obstetric complications may have different long term implications in ASD (Kolevzon et al., 2007; Maimburg et al., 2002). More recent research has generally been conducted using large scale population based studies, with recognition of individual obstetric complications and this should give a better indication of the pre- and peri-natal risk factors in ASD.

It has been suggested that maternal circumstances during pregnancy and prenatal exposure to exogenous substances during a critical developmental period, possibly pre-conception or during the first trimester, may be an important in the development of ASD (Newschaffer et al., 2002; Glasson et al., 2004; Maimburg et al., 2002). Maternal hypothyroidism, thalidomide, valporic acid, cocaine, alcohol use and exposure to rubella have all been associated with increased ASD (Hultman et al., 2002; Rutter, 2005; Newschaffer et al., 2002) though epidemiological studies have failed to find any one of these factors as common to all cases on of ASD (Rutter, 2005).

Independent of the increased risk for ASD as a consequence of exposure to a substance prenatally, is the research which has investigated the naturally occurring pre- and peri-natal risk

factors for ASD. It has been noted that there is an increased incidence of ASD in children who have been in intensive care postnatally (Hultman et al., 2002), which suggests that circumstances, either pre-natally, during labour, delivery or post-natally, are increasing the risk of ASD.

A factor consistently reported as increasing the risk of ASD is advanced maternal age (Croen et al., 2007; Glasson et al., 2004; Hultman et al., 2002; Kolevzon et al., 2007; Larsson et al., 2005). The association between an older mother and increased incidence of ASD is thought to be due to a greater risk of pregnancy complications, particularly during labour and delivery, with increasing age (Glasson et al., 2004; Kolevzon et al., 2007). Increased paternal age has also been reported as a significant risk factor for ASD (Glasson et al., 2004; Kolevzon et al., 2007), however, researchers have noted that this is most likely to be due to the associated increase in maternal age (Kolevzon et al., 2007).

A second peri-natal factor found to be associated with an increased incidence of ASD is low birth weight (Maimburg et al., 2006; Larsson et al., 2005). A group of children born with low birth weight, as discussed in previous sections, is likely to be heterogenous. In some, the low birth weight may be caused by growth restriction in utero, while in others it will be as a consequence of being born prematurely. Low birth weight generally has been reported to be associated with an increase in ASD (Maimburg et al., 2006; Larsson et al., 2005), with research suggesting that both those born low birth weight due to prematurity (Williams, et al., 2007; Cryan et al., 1996; Larsson et al., 2005) and those born low birth weight due to growth restriction (Larsson et al., 2005; Hultman et al., 2002) are at an increased risk of ASD. There is however research which suggests that prematurity alone is not a risk factor for ASD (Burd et al., 1999; Juul-Dam, et al., 2001).

In those born low birth weight as a consequence of IUGR, with birth weight which places them below the 10th centile for gestational age and therefore small for gestational age (SGA), there has been found to be a two fold increase in the incidence of ASD (Hultman et al., 2002; Larsson et al., 2005) and this was found to remain significant even after other factors known to impact on increased ASD incidence were controlled (Hultman et al., 2002).

The actual mechanism by which SGA status is related to the increased incidence of ASD remains unclear. Small size at birth may be due to the foetus being unhealthy due to a genetic or

environmental insult, with ASD being an additional complication of the insult. Alternatively complications as a result of being born SGA may be directly responsible for the increased incidence of ASD.

Low apgar score at 5 minutes (Hultman et al., 2002; Kolevzon et al., 2007), threatened abortion, maternal bleeding (Glasson et al., 2004) and caesarean section (Maimburg et al., 2006; Glasson et al., 2004) have also been associated with an increased risk of ASD. As with SGA status at birth, it is not known whether these are an indirect cause of ASD or a reaction of an already unhealthy foetus.

The post natal complication which has been found to have the highest correlation with ASD is epilepsy (Clarke et al., 2005; Levison et al., 2007). It has been estimated that approximately one third of children with ASD will have experienced a seizure by adolescence (Olson et al., 1988; Volkmar et al., 1990) and between 5-38% of children with ASD will have comorbid epilepsy (Rossi et al., 1995; Tuchman & Rapin, 2002; Danielsson et al., 2005). As already mentioned in this review, the seizures experienced by children with TSC are thought to be important in the high correlation between TSC and ASD (Wiznitzer et al., 2005).

The Mumps Measles and Rubella (MMR) immunisation was reported to be associated with increased levels of ASD in the research of Wakefield et al., (1999; 1998). This research led to a large body of research being conducted to test this association but to date there has been no research replicating the findings of Wakefield et al., (Wilson et al., 2003; DeStefano & Thompson, 2004; Baird et al., 2008).

1.5.5.3 Summary of causes of ASD

There is a strong genetic indication in ASD, however genetics can not completely explain all incidences of ASD. Genetic syndromes, such as TSC and fragile X, have been found to correlate with an increased incidence of ASD, though in these cases changing brain neuropathology due to the syndrome, and not the genetics are thought to cause the raised incidence of ASD.

Peri-natal risk factors for ASD include, increased maternal age, low apgar score at five minutes, caesarean section delivery and low birth weight. Both low birth weight as a consequence of prematurity and IUGR have been found to be associated with an increased risk of ASD. Whether low

birth weight is a consequence of an underlying pathology which also causes ASD, or ASD is a consequence of low birth weight complications remains unclear.

A strong correlation has been found between ASD and epilepsy, though as with low birth weight, it remains unclear whether ASD is a consequence of neuronal damage caused by epileptic seizures, or an underlying neuropathology is causing both ASD and epilepsy.

1.5.6. Long term consequences of ASD

As ASD is a spectrum, there is a wide range of abilities and behaviours of those who would receive an ASD diagnosis. At one end of the spectrum are those with severe behavioural disturbance and profound learning disabilities, while at the other, those with a diagnosis of ASD have been found to display age appropriate independent functioning. A review of the long term consequences of those at the most severe end of the spectrum would not be relevant as it is anticipated that children with RSS, who are found to have ASD, will be high functioning. Therefore, a brief review of the consequences for children with AS and HFAD only, will be made.

Children with HFAD and AS are at high risk of difficulties in social situations, due in part, to their lack of social skills, which are essential to form meaningful relationships, and often appear clumsy and inappropriate. Children with ASD have been found to be less likely to initiate peer interaction, spend less time interacting with peers, have low quality interactions and spend large amounts of time in non-social play (Lord & Magill-Evans, 1995; McGee et al., 1997; Sigmund & Ruskin, 1999). They display an inability to read social cues and emotions and respond to them incorrectly, often reacting in a fast and impulsive retaliatory manner (Sofronoff et al., 2007).

Children with ASD often have circumscribed interests, normally with facts and trivia, and they are often unable to inhibit these interests in order to actively participate in school, home life or other social situations (South, Ozonoff & McMahon, 2005). In addition, they are reported to have poor organisational and time management skills (Sofronoff et al., 2005) and sensory abnormalities (O'Neil, 1995; Harrison & Hare, 2004).

The APA (2000) recognise that there is an association between AS and HFAD and secondary mood disorders, with anxiety and anger both noted as occurring at a high rate (Sofronoff et al., 2005; 2007; Kim et al., 2000; Green et al., 2000). This association is most likely a reaction to the poor social

skills, where they are unable to read social cues and express their feelings in words (Sofronoff et al., 2007) but may also be related to their sensory sensitivity which is likely to increase anxiety and frustration (Sofronoff et al., 2005). Cognitive Behavioural Therapy (CBT) has been found to be effective in reducing the incidence of anxiety (Sofronoff et al., 2005) and anger (Sofronoff et al., 2007) in children with AS and HFAD, which can be seen to improve quality of life. Social skills training has also been used for many years to help children with AS and HFAD, however, the usefulness of this treatment has still to be proven unequivocally (Rao et al., 2007; Williams-White et al., 2006).

Although ASD is a life long condition, the long term prognosis of those with ASD is now much better than it would have been 20-30 years ago (Billstedt et al., 2005), due to the improved understanding of ASD and its potential consequences.

1.5.7. Section Summary

The incidence of ASD has increased in the last decade and recent estimates have reported that 67 in every 10,000 children will receive a diagnosis of ASD, compared to early reported incidence of 4-5 in 10,000.

The best established risk factor for ASD is one of genetics (Rutter, 2005), though the pattern of inheritance is not simple, with many genes thought to be involved. Genetics can not completely account for all instances of ASD and many pre- and peri-natal factors have been found to correlate with increased ASD incidence. Those born SGA, as children with RSS are, have been found to be at a two fold increased risk of ASD, though the mechanism for this association remains poorly understood.

ASD are life long, and there are implications of having an ASD even at the high functioning end of the spectrum. There is an improved prognosis for those with ASD now, with improved understanding of the condition

1.6. Short Stature

The first two aims of this thesis were to create cognitive and behavioural profiles of children with RSS. The third aim was to create a psychosocial profile, assessing self esteem and body image attitude of children with RSS, and assessing how others view children with RSS. One of the main symptoms of RSS is short stature, therefore a literature review of short stature and the potential

psychosocial consequences of short stature was conducted.

1.6.1. What is Short Stature (SS)?

In the USA, children with idiopathic short stature (ISS), with current height and growth 2SD below the mean for age, are eligible to receive Growth Hormone Treatment (GHT) to potentially increase their adult height. There is currently no UK product licence for the use of GH with ISS children. 2SD below the mean, however, is the nearest to a numerical definition of short stature. It is assumed that children with heights below this will encounter problems, including, low self esteem, social isolation, withdrawal, immaturity, body image disturbance and that they will socialise with those in a younger age group (Gordon, 1982, Sandberg et al, 2004, Sandberg et al, 1994, Ross et al, 2004).

1.6.2. The short stature stereotype

Short stature as a disadvantage is a long held stereotyped belief. Research with adults and children, has shown that taller adults are expected to be in higher paid jobs, to be earning a higher salary and have more positive attributes than their short stature counterparts (Gilmour & Skuse, 1996; Clopper, 1994). The assumption, that stature and status are connected, has real life support, tall men were found to receive a 4-6% higher salary than their counterparts, and were also more likely to be married (Harper, 2000, Loh, 1993). The effect of height on perceptions of women is different from that of men, no relationship has been found between height and wage received in women, and women have actually been found to be less likely to be married if they were tall (Harper, 2000). These findings highlight the important role of gender in height related attributions and a point of caution when generalising single sex findings to the whole short stature population. It has been demonstrated that the actual role of height in our attributions becomes less important, although still playing a role, as other verbal and non-verbal factors are taken in to account (Sandberg ; Voss, 2006).

Law (1987) states that it is widely assumed that short children are seen differently by adults and peers, much as adults are. Findings from studies carried out with short stature children include teachers reporting taller children as more mature than their counterparts and having height dependent scholastic expectations (Wake, Coghlan & Hesketh, 2000). In a 1996 survey of American physicians, 56% said that children with short stature were disadvantaged and that their quality of life would be

improved with GHT (Cuttler et al, 1996). Mothers rated tall boys and girls as more competent than those who were average height or short (Eisenberg et al, 1984) with shorter individuals being seen as physically weaker (Holmes, 1982). Short children are consistently seen as younger than their peers and are treated in a way which is appropriate for their height, rather than their age (Alley, 1983; Lerner, 1969).

A large number of children with idiopathic short stature (ISS) are now referred to growth clinics for assessment and treatment for short stature. In 2002, in the USA, it was estimated that 1 in 3 children receiving growth hormone treatment (GHT) had a diagnosis of ISS (Sandberg & Voss, 2002). Behavioural and cognitive problems are often reported in children with short stature, with difficulties being attributed to overprotection and aversive experiences related to their stature (Stabler et al, 1998), although whether behavioural and cognitive problems can actually be attributed to short stature experience remains to be justified.

There is a significantly greater number of males than females with ISS referred to clinics for assessment and treatment for their SS, with the mean height of the males at referral significantly greater than the female (Grimberg, Kutikov, Couchirra, 2005, Sandberg, Brook & Campos, 1994, Ross et al, 2004). The male bias in referral may be due to the stereotypical belief that short stature is a greater disadvantage in males, or because short stature may cause more behavioural problems in males (Sandberg, 2004; Grimberg, 2005), although the latter is thought to be unlikely (Sandberg, 2004).

The debate regarding the use of recombinant GHT with children who are short has led to a large body of research into the consequences of short stature, and whether or not it should be seen as a illness requiring treatment (Gill, 2006; Ulph, Betts, Mulligan & Stratford, 2004; Voss, 2000). The findings of this research not only allow debate regarding GHT use but also give a better understanding of the problems faced by children with short stature, such as those with Russell Silver Syndrome.

1.6.3. Psychosocial effects of short stature in children

Historically, there has been research to support the view that short stature children have psychosocial problems, including, lower social competence and more social problems and that they were found to be functioning either academically normally or below normal (see Visser-van Balen,

Sinnema & Geenan, 2006 for review). Reported problems to the paediatrician include stigmatization, juvenilisation, immaturity and unassertiveness (Voss & Sandberg, 2004).

1.6.3.1. Referred children

Firstly, looking at studies working with clinic referred populations only, more behaviour problems (Gordon et al, 1982; Sandberg et al, 1994; Stabler et al, 1998;), lower intelligence and academic achievement (Stabler et al, 1994; Gilmour & Skuse, 1996; Stabler et al, 1998; Stathis et al, 1999) and lower self esteem (Gordon et al, 1982, Gilmour & Skuse, 1996) have been found in those with short stature than in controls. These findings fit with the expectation that short stature is a disadvantage, however, these findings should be taken with caution. There are limitations of studies which work with referred populations only; it is unlikely that a child would be referred for assessment of short stature unless there was an additional cause for concern e.g. behavioural problems, low academic achievement and low self esteem (Stabler & Frank, 1998). That these problems have been caused by experience relating to short stature is presumed by the researchers, but cannot be known for certain. This is a particular problem in older research, such as that of Gordon et al (1982), as at the time that the research was conducted, only human growth hormone treatment was available, therefore, only those with the greatest cause for concern would have been referred for potential treatment (Sandberg & Voss, 2002). Additionally, as already established, there is a male bias in referrals (Grimberg et al, 2005, Kranzler et al, 2000), meaning that referred sample studies are also likely to have a male bias and as short stature is perceived differently in males and females, these data are therefore difficult to generalise to the whole short stature population.

Kranzler et al's (2000) paper addresses the problem of referral bias in short stature research, by comparing referred and non-referred short stature groups. Referred and non-referred groups were not found to differ significantly from controls with regards to intelligence. Adaptive and behavioural problems however displayed a referral bias, with the referred group displaying significantly more problem behaviours than non-referred or control children. Busschbach et al (1998) also addressed the problem of referral bias, with two groups of short adults, those who had been referred for treatment for short stature in childhood and those who had not. It was found that those who had been referred had poorer coping skills and felt much more that their short stature was to blame for any social

disadvantage.

1.6.3.2. Population studies

The Wessex growth study is a major longitudinal study of the effects of stature in a community sample. It started in 1989, with children aged 5-6 years living in the Wessex area of the UK. The physical, social, educational and psychological development of the children recruited has since been monitored longitudinally. 140 short normal children (below the 3rd centile) were recruited from the general population and followed up at 7-8 years, 12-13 years and 18-20 years.

The first stage of assessment, at 7-8 years (Voss et al, 1989), found no difference between short and normal height children in terms of physical, social, educational and psychological development. A small difference could be seen for teacher's ratings of attainment, but this could be attributed to social class.

The follow up at 12-13 years (Downie et al, 1997), found that, on the majority of scales, the two groups continued to show no difference in scores. There was a significantly lower mean IQ found in the short stature group, but this again could be attributed to social class differences. Additionally, while those who were short did show more body dissatisfaction; this was not found to impact on self esteem. In addition to longitudinal testing, Voss and Mulligan (2000) monitored the effect of short stature on bullying at school. They found that more short boys reported being bullied, girls did not differ, a finding also observed by Erling *et al.*, (2004). And, while both males and females were found to have as many friends as their taller peers they also reported spending more time alone.

In the most recent follow up, age 18-19 years, (Ulph, Betts, Mulligan & Stratford, 2004) the differences between the two groups remained minimal. Short stature was found to have little effect on psychosocial development; gender and personality were found to have a much greater influence.

It has been found, that how children perceive themselves in terms of their stature is more influential than their actual height measurements (Voss, 2006, Theunissen et al, 2004, Hunt et al, 2000; Erling et al, 2004), a child who is above -2SD but is substantially shorter than any other family member is likely to perceive themselves as short, while a child of the same height with relatively short parents, would probably see themselves as average. Despite attempts to clarify whether short stature is a disadvantage, and if so at what height, short stature remains to the greater extent subjective.

1.6.4. Short stature and small for gestational age

Approximately 13-14% of children born SGA do not show catch up growth by two years of age, these are at high risk of remaining short in to adulthood (Karlberg & Albertsson-Wikland, 1995; van der Reijden-Lakeman, 1996; Saenger, 2007) with 7.9% of children who were born SGA were found to remain below -2SD for their height at the age of 18 years (Karlberg & Albertsson-Wikland, 1995). Lee et al (2003) reviewed studies with SGA infants in the context of the long term problems of short stature, however, they noted that any research findings with children born SGA with continued short stature could not be attributed to the short stature alone. They failed to find a study which adequately compared those born SGA with short stature and those born Average for Gestational Age (AGA) with short stature. SGA and short stature are intrinsically linked, but neither the studies looking at the long term consequences of being born SGA, or those investigating short stature, routinely control for the other factor. This highlights an area for future research. At present our knowledge of how short stature and SGA can be separated with regards to growth and development remains flawed.

1.6.5 Section Summary

Short stature has long been thought of as a disadvantage in children and adults. Studies with participants recruited through clinic referrals support this presumption, with lower self esteem, lower cognitive ability and more behavioural problems in short stature children. Referral studies are likely to over represent the problems seen in short stature children, due to sample bias to the children who already display problematic behaviours. The Wessex growth study found few differences between short and normal height children at three different ages of assessment, in terms of behavioural, intellectual and psychosocial development. It is thought actual height plays less of a role in problems which have been associated with short stature, than does perceived height.

1.7 Face Shape

A second feature seen in children with RSS, is a characteristic face shape, with many similarities to the face shape of a baby. To guide expectations of how children with RSS will view their facial appearance, and the potential impact this could be having on their self esteem and body image attitude, a review of baby face shape literature was conducted.

1.7.1. The RSS face shape

Children with RSS display characteristic facial features which were first documented by Russell (1954). While most of the RSS child's physical measurements are smaller than expected at birth and remain so, the size of their cranium is preserved. This gives the impression of a large head and what is referred to in the literature as a "triangular face" (Plotts, 2000; Hitchins, Stanier, Preece & Moore, 2001; Anderson, Viskochil, O'Gorman & Gonzales, 2002; Preece *et al.*, 1997; Lai, Skuse, Stanhope & Hindmarsh, 1994; Perkins & Hoang-Xuan, 2002; Ounap, Reimand, Magi & Bartsch, 2004). Children with RSS have a small lower face, particularly jaw, often encountering orthodontic problems. A secondary feature of their small lower face, is that the eyes appear larger and the ears lower set in the plain of the face, this is exacerbated by the small amount of subcutaneous fat that these children have.

1.7.2. Baby face shape

Large, round eyes and a narrow chin have been found to be the best indicators of a baby-faced appearance (Berry & McArthur, 1985, Zebrowitz-McArthur & Berry, 1987) and this is a cross culturally stable effect (Zebrowitz-McArthur & Berry, 1987). There has been found to be some male and female variability in features considered indicative of a baby's face, with eye size being more important in male ratings and nosebridge size in females (Zebrowitz & Montepare, 1992).

Facial features seen in both babies and children with RSS, include large eyes, eyes in the centre of the vertical plane of the face, and a large protruding cranium (Berry & McArthur, 1985, Zebrowitz-McArthur & Berry, 1987, Zebrowitz & Montepare, 1992, Masip, Garrido & Herrero, 2004). RSS children, however, do not have a curved face which is a key feature of a baby's face, though not as important as the eyes and a narrow chin (Berry & McArthur, 1985).

The similarity in features between those with RSS and a baby makes it relevant to review literature which appraises how people view those with baby-like faces. Understanding how people perceive those with baby-like features should give an indication of how those with RSS features are perceived.

1.7.3. Facial stereotypes

It is well established in the literature, that facial affordances, that is visual cues, guide what we think about others and this, in turn, can guide our expectations of them (Santos & Young, 2005). This idea is founded on ecological theory, that is, the assumption that perceptible attributes provide information about the person's behavioural traits (Masip *et al.*, 2004). Over-generalization of a rule based on physical appearance, could potentially lead to the prediction of incorrect behavioural traits, such as, weak, baby-like, attributes expected in an adult with a baby-like face (Zebrowitz-McArthur & Berry, 1987, Zebrowitz, Fellous, Mignault & Andreoletti, 2003). Despite the inconvenience of overgeneralization it is thought to be more advantageous than undergeneralization (Zebrowitz *et al.*, 2003), for example, there is an increased chance of survival if weakness is over-predicted rather than under-predicted.

Verbal and non-verbal factors, other than facial affordances, are also known to play a crucial role in our decisions about trait attributions, and these, as well as facial affordances, can be influential after only a brief period of exposure (Zebrowitz, Murphy, Hall & Rhodes, 2002; Friedman, Oltmans, Gleason & Turkheimer, 2006). The largest effect, however, is seen when several factors, verbal and non-verbal, act in combination (Friedman *et al.*, 2006).

Research focussing on facial features as cues to personality traits, has historically centred on attractiveness and specifically the "halo effect". People tend to give more positive attributes to attractive individuals, specifically, likeability, popularity, extraversion, and intelligence in particular have been rated as higher in those seen as more attractive (Paunonen, Ewan, Earthy, Lefave & Goldberg, 1999). The judgement of attractiveness is thought to be innate, with infants as young as 4 months showing a preference for attractive faces (Langlois, Ritter, Roggman & Vaughn, 1991). Facial symmetry and shape, and eye size and spacing have been found to be particularly important in decisions of attractiveness (Paunonen *et al.*, 1999).

The eye area has been found to particularly important in judgements about how baby faced a person is as well as in decisions of attractiveness. Attractiveness and baby facedness, however, have not been found to be synonymous (Paunonen *et al.*, 1999, Berry & McArthur, 1985; Berry & Brownlow, 1989; Masip *et al.*, 2004). Paunonen *et al.*, (1999) asked participants to rate photographs

on a number of characteristics, four physical features (attractiveness, babyface, masculinity, physical strength) and thirteen personality traits (inc. nurturance, extraversion, honesty and empathy). Babyfacedness and attractiveness were found to be mediating factors when making decisions about personality traits, although attractiveness was not found to be as influential on trait attributions as babyfacedness. Additionally, the traits that were found to be the highest in those rated the most babyfaced were different to those rated as highest in attractive individuals.

1.7.3.1. The baby face stereotype

The facial features seen in babies are such that they elicit a protective response from caregivers, thereby increasing the chance of survival (Lorenz, 1943; Masip et al., 2004; Alley, 1988). According to ecological theory and overgeneralization, traits of babies, such as naivety and physical weakness, would be attributed to children and adults (Berry & Brownlow, 1989, Zebrowtiz et al., 2003) who facially resemble babies and, in turn, those who physically resemble babies will be treated as if they have baby-like traits.

Research carried out with adult photographic stimuli, has found that a rating of how babyfaced a person is, is positively correlated with ratings of warmth, honesty, physical weakness, submissiveness, naivety, kindness; with baby faced individuals thought to have more childlike qualities (Berry & McArthur, 1985; Masip et al, 2004).

The traits attributed to individuals have been found to be independent of perceived age and remain constant across the lifespan, with baby faced individuals being perceived as more naïve, weaker and warmer no matter what their actual age (Zebrowitz & Montepare, 1992; Zebrowitz, Olson & Hoffman, 1993; Berry & McArthur, 1985; Berry & Brownlow, 1989; Masip et al., 2004).

Research carried out with child photographic stimuli has found that those who were babyfaced were perceived by adults as being less capable in household chores than their peers, despite adults being told that all children in the photographs were the same age. Surprisingly though, the variation in the household chores assigned differed according to the cognitive demands of the task rather than the physical demands (Zebrowitz , Kendall, Tackett & Fafel, 1991).

It has also been demonstrated that baby-facedness is influential on punishment given to children. Those with babyish facial features were given more severe punishments than mature faced

individuals when the behaviour did not fit with the stereotype expected behaviours, e.g. physical assault (Langlois et al., 1996). Less intent, however, was assigned to baby faced individuals and they were found to be given more benefit of the doubt (Zebrowitz & Lee, 1999; Zebrowitz et al., 1991; Zebrowitz, Collins & Dutta, 1998¹).

In a sample of children who had shown delinquent behaviour, those who were babyfaced were found to have had less maternal supervision, this was thought to be because honesty, which is known to be rated higher in those with a baby face, was the most salient feature to the mother. The opposite effect was found when studying a group of non-delinquent children, those who were more babyfaced had the highest level of maternal supervision, in this case naivety was thought to be the most salient feature to mothers (Zebrowitz & Lee, 1999).

There is support for the detection of baby face like characteristics being innate. Korean students, who had had little exposure to Western faces, were found to perceive baby-face characteristics in a Western face, in a comparable way to Americans on all dimensions (Zebrowitz & Berry, 1987). A preference for photographs of infants over older children and adults has been shown in children even as young as 4 months (McCall & Kennedy, 1980; Alley, 1988).

The actual personality characteristics of those with a baby-faced appearance, have been found to fit well with those expected, supporting a self fulfilling prophecy effect (Zebrowitz et al., 1998¹, Berry & Brownlow, 1989). There is also, however, evidence of behaviour being self defeating, that is those with a baby faced appearance behave in a way which is opposite to expectations (Zebrowitz et al., 1998¹). This self defeating effect has only been found in males, and is shown particularly strongly in adolescence. Social economic status was found to play an important mediatory role, those with a low SES and a baby-face were found to achieve less years of education than mature faced peers, while those with a baby-face and high economic status achieved more years of education than their mature faced peers (Zebrowitz, Andreolotti, Collins, Lee & Blumenthal, 1998²).

1.7.4. Section Summary

Children with a diagnosis of RSS display facial features with many similarities to the facial features seen in babies and infants. In infants and babies these features are intended to provoke protective feelings in caregivers to aid survival. Adults and children who have baby like facial

features have been found to be rated higher on traits associated with babies and infants, this is a demonstration of an overgeneralization of traits based on physical appearance.

The effect of being attributed infantile traits based on physical appearance has been found to have an effect on personality development, though this is mediated by social class and gender.

1.8 Broad aims of the present thesis

The overall aim of this thesis is to understand better the cognitive, behavioural and psychosocial profile of children with RSS. The thesis is constructed of three chapters, each assessing one of the above factors, with a final summary integrating the findings from the three previous chapters.

The first empirical chapter will consist of a systematic review of the long term cognitive effects of being born SGA at term and a study comparing RSS and control children for cognitive ability. Combining the findings from the systematic review and the research study, it is thought that any cognitive deficits seen in children with RSS, can be attributed to their SGA status, or this factor can be ruled out as the main cause of cognitive difficulties.

The second chapter will investigate the behavioural profile of children with RSS. The first section reports a behavioural screening questionnaire, but further to this a more in depth investigation will be conducted assessing ADHD and ASD in children with RSS.

The third chapter will investigate psychosocial factors in RSS, specifically looking at their perceptions of their height, weight and face shape and this impact this has on their self esteem. Further to this a study will be conducted looking at how others perceive the salient features of RSS, short stature and phenotypical face shape, and how this impacts on their trait attributions.

The literature review conducted here revealed that there are factors in different areas being investigated which may have some commonality in cause, for example it is known that being born SGA can be important in both the development of ADHD and ASD and has also been found to be a factor in reduced cognitive ability. What remains important is to discover typical profiles, for example if a child has increased levels of ADHD are these also the RSS children more likely to have ASD and cognitive difficulties, or are these factors independent?

The present thesis has potential clinical and educational implications for children with RSS. Generating a better understanding of the long term development of children with RSS will mean that parents, teachers and physicians will be aware of potential complications, and interventions can be put in to place in order to reduce the long term impact of these consequences.

Chapter 2

General Methodology

2.1 Introduction to general methodology chapter

This chapter presents the research design and strategy for this thesis. A description of the research samples and questionnaire measures used in this thesis will be followed by a brief description of the general procedure and data analysis strategy. As Study 7 was conducted with a different methodology and research sample to the rest of the thesis this will be briefly described separately.

2.2 Research design and strategy

The current thesis comprises three data chapters. The first chapter includes a systematic review of the long term consequences of being born small for gestational age at term, and two empirical studies, one comparing the cognitive and behavioural profile of children with RSS with age matched children born SGA without RSS and a second comparing the cognitive abilities of a larger group of children with RSS and an age matched control group. Findings from the systematic review were used to help guide the hypothesis and discussion of the empirical studies in this chapter.

The aim of the second data chapter was to assess the behavioural profile of children with RSS. This was achieved over two studies. The first study gives an overview of the behavioural profile of children with RSS relative to a control group and investigates ADHD in children with RSS. The second study was conducted further to parental and physician reports, and investigates the incidence and potential causes of Autistic Spectrum Disorder (ASD) in children with RSS.

The final empirical chapter of this thesis investigates the psychosocial profile of children with RSS. Study 6 was conducted with the same research sample as in the rest of this thesis, and investigated the body image and self esteem of children with RSS, relative to the control sample. The final study, Study 7, assessed how others perceived children with RSS typical features, specifically assessing how these features impacted on the physical and personality trait attributions of children and adults.

2.3 Participant recruitment and demographics

The main aim of the present thesis was to understand better the cognitive, behavioural and psychosocial development of children with RSS. The majority of this thesis is made up of empirical

studies conducted with a relatively large sample of RSS children in comparison to an age matched control group. An additional study was conducted comparing a sub-group of RSS children recruited, with age matched children born IUGR/SGA without RSS. It was initially anticipated that this further control group would be used for all studies, however, it proved difficult to recruit a sufficiently large IUGR/SGA group to make this viable.

Study 7 makes up an additional investigation into the way others see those with RSS, therefore the sample included in this study is not clinical, but general population. The sample used in this study is discussed separately.

2.3.1 Clinical group (Russell Silver Syndrome)

Parents of children aged 5-16 years with a diagnosis of Russell Silver Syndrome were recruited in three ways. Initially RSS specific information packs, including information sheet consent form, brief demographic questionnaire and prepaid envelope (appendix A), were sent to all members of the Child Growth Foundation (CGF) aged 5-16 with a diagnosis of RSS. Age appropriate information sheets were included for the children contacted, one for children over 10 years (appendix B) and one for children under 10 years (appendix C).

The researcher also regularly attended the growth clinic at Birmingham Children's Hospital. It was anticipated that potential participants with a diagnosis of RSS would be told about the research by their doctor during their appointment, if they displayed an interest in participating, the researcher would meet with them following the appointment and provide them with an information pack, identical to those distributed through the CGF. During the time the researcher spent at the clinics, only those with RSS who had consented to participate attended the clinic and no further participants were recruited in this way. The third method of recruitment was through the Nand through the NESGAS research. This is a multi-centre (Birmingham, Cambridge, and Glasgow) project investigating GHT in children born SGA, research assistants at all three sites were contacted and asked to distribute information packs, about this research, to already recruited participants aged 5-16 years.

Response rate

In total, 42 children with RSS were sent information packs about the research through the CGF, 28 children with RSS consented to participate in the research. Four participants that consented

to participate did not respond when sent the questionnaire pack, which formed the first part of the study, and after a repeat sending, were excluded from the research, leaving a total RSS group of 24 children.

One child recruited as part of the RSS group emigrated after consenting to participate, the family did complete the questionnaire stage of the research, but were excluded from the stages of the research which required a home visit.

2.3.2 Control Group

Children born within a year of those in the RSS group were considered as age matched control participants. Any child with a serious organic disorder, serious brain damage or dwarfism caused by disorders other than those tested were excluded from the research, as were those who had experienced a traumatic event that may have led to emotional problems. Control participant's current height had to be greater than the 10th centile, using standardised growth charts and their birth weight greater than the 10th centile for gestational age. Both the child and parent had to understand written and verbal information in English to participate in the research.

Recruitment of age matched control children was difficult and several different methodologies were used.

- Head teachers of approximately 40 infant, junior, middle and secondary schools local to the university were sent a cover letter, information pack about the research and a consent form (see appendix G). The head teacher returned the completed consent form if they were happy to distribute information about the research to pupils and parents of their school. After receiving a completed consent form, the researcher would visit the school and explain to explain about the research and deliver information packs for distribution (appendices H, I, J). One mixed primary school in a rural area and one infant and one junior school in the north of Birmingham responded and participated from this recruitment (see table 2.1 for response rate).
- Due to the low response rate the initial stage of recruitment was revised. A one page flyer was designed (see appendix K) briefly explaining the nature of the research being conducted, with

contact details of the researcher and offering a £5 book voucher to all those that participated. Primary, Infant and Middle schools in the Worcestershire were contacted by phone and asked to consent to distributing the flyers to all their pupils. Two middle schools and three primary schools agreed and in total approximately 350 flyers were distributed (see table 2.1 for response rate).

- A colleague within the department who had also had difficulties recruiting a control sample was approached. As part of their research, control participants had consented to being contacted about further research in the department and a further 20 potential participants were contacted about the current research (see table 2.1 for response rate).
- Participants in the clinical groups were contacted. They were asked if they were able to distribute information about the research to friends and family with children. It was thought that knowing someone with an experience of RSS may make people more inclined to participate (see table 2.1 for response rate).
- The remainder of control matched participants were recruited through sending e-mails around the School of Psychology at the University of Birmingham and by word of mouth through friends and family of the researcher and members of the department (see table 2.1 for response rate).

Table 2.1: Response rate for control group recruitment

	Flyers sent	Response rate	Information packs sent	Response rate	Total age matched sample
Full information pack	-	-	440	10 (2.3%)	7
Flyer	350	5 (1.4%)	5	3 (60%)	3
Participants from previous research	-	-	20	2 (10%)	1
Friends and family of clinical group	-	-	28	3 (10.7%)	3
e-mail and word of mouth	-	-	10	10 (100%)	10

Four children were excluded from the control group as they could not be age matched to any of those participants recruited as part of the RSS clinical group.

Although RSS and control groups were not matched for SES and parental education, they were compared on these factors once recruited. If they were found to differ significantly then it would be important throughout the thesis to control for these factors as they are known to have an independent effect on factors being assessed, including cognitive abilities (Shenkin, Starr, Pattie, Rush, Whalley & Deary, 2001) and ADHD (Offord et al., 1992; Barkley, 1990). Parental occupations were used as an indication of SES, these were coded and combined to give a mean SES score for each child following the guidelines of Rose & Pevalin (2005). Maternal and paternal highest level of education were also categorised with numerical values and the two groups compared. The two groups were not found to differ significantly (see table) therefore throughout the thesis it can be assumed that any group differences were not caused by any of these factors.

Table 2.2: Comparison of RSS and Control group participants for SES, maternal education and paternal education.

	N	SES M (SD)	Maternal Education M (SD)	Paternal Education M (SD)
Russell Silver Syndrome	23 (11 male, 12 female)	2.24 (1.37)	3.29 (1.23)	3.19 (1.40)
Control	23 (11 male, 12 female)	2.38 (0.80)	3.52 (0.98)	2.81 (1.36)
		T=0.41, p=0.68	T=0.69, p=0.49	T=0.89, p=0.38

2.4 Standardised measures used in empirical studies

2.4.1 Cognitive measure

2.4.1.1 British Ability Scale – II (BAS-II; Elliott, Smith & McCulloch, 1996)

The BAS-II is a hierarchical measure of cognitive ability, which can be used with children from 2 years 6 months, to 17 years 11 months. The BAS- II is available in two versions, the early years battery, which can be used with children 2 years 6 months through to 7 years 11 months, and the school age battery, which can be used with children aged 5 years through to 17 years 11 months.

The child completes six core scales in both the early years and school age batteries. For the early years battery, verbal ability, a pictorial reasoning ability and a spatial ability scores can be calculated from the core scale scores. In the school age battery the pictorial reasoning ability score is

replaced by a non-verbal score. Table 2.2 summarises the clusters and the tasks which contribute, for the early years and school age batteries of the BAS-II.

Table 2.3: Summary of cluster components BAS-II

Early Years		School Age	
Task	Cluster	Task	Cluster
Verbal comprehension	Verbal Ability	Word Definitions	Verbal Ability
Naming vocabulary		Verbal Similarities	
Picture similarities	Pictorial Reasoning Ability	Matrices	Non-verbal Ability
Early number concepts		Quantitative Reasoning	
Copying	Spatial Ability	Recall of Design	Spatial Ability
Pattern Construction		Pattern Construction	

Children completed the BAS-II with the chief investigator, in a quiet distraction free environment. The assessor sat at right angles to the child, and explained each of the tasks, using the provided examples.

For each task, the start point question was according to chronological age. The child completed all tasks to a set stop point, number of items completed successfully at this point dictated whether further items should be completed. If the child was getting items incorrect consistently, the assessor moved back to items from an earlier chronological age.

Total raw scores for each task were calculated and for the majority of tasks, this was the total number of correct answers given for that task. For recall of designs (school age battery) and copying (early years battery), scoring was conducted after testing, with points given for drawing accuracy. For pattern construction (early years and school age battery), scores were calculated based on speed of task completion. For all tasks total raw scores were converted to ability scores, based on difficulty of items attempted, and then to age appropriate t-scores and percentiles using tables provided in the BAS-II administration and scoring manual (Elliott et al., 1996).

Cluster scores, verbal ability, non-verbal ability/pictorial reasoning ability and spatial ability, were calculated by summing t-scores for the tasks which make up each of the clusters (see table 2.2). Total cluster scores were then converted to standard scores using the tables provided in the BAS-II administration and scoring manual (Elliott et al., 1996). To calculate the General Cognitive Ability (GCA), t-scores for all the tasks were summed and converted to standard scores as above.

In addition to the core scales of the BAS-II, the measure includes diagnostic scales designed to measure aspects of the child's ability not thought to contribute directly to their GCA (Elliott et al., 1996). Table 2.4 summarises the diagnostic measures of the BAS-II.

Table 2.4: Summary of diagnostic scales of the BAS-II with brief summary of which abilities each scale is measuring (adapted from BAS-II, technical manual)

EARLY YEARS BATTERY	WHAT SCALE MEASURES
Matching letter like forms	Visual discrimination and awareness of spatial orientation
Recall of digits forward	Short term auditory memory, concentration and attention.
Recognition of pictures	Short term visual recognition memory, visual scanning efficiency, attention to visual detail.
Recall of objects (verbal)	Short and intermediate term visual-verbal recall, verbal working memory, integration of visual and verbal information.
Recall of objects (spatial)	Short and intermediate term visual recall, visuo-spatial working memory.
SCHOOL AGE BATTERY	
Speed of Information processing	Speed of performing simple mental operations, ability to work under pressure, sequential strategies for making comparisons.
Recall of digits forward	As above
Recall of digits backward	Use of strategies to convert digits, short-term auditory memory, concentration and attention
Recognition of pictures	As above
Recall of objects (immediate verbal and spatial)	As above
Recall of objects (delayed verbal and spatial).	As above

The reliability, validity and factor structure of the BAS-II has been established with UK samples (Elliott et al., 1996) and there is evidence that the scale has been used with other syndrome

groups (Karmiloff et al., 2003) and disorders (Marlow, 2005; Keen & Ward, 2004). The BAS-II was designed so that individual tasks and clusters could be used independently, and there is evidence of this in the literature (Oliver & Plomin, 2007). Strong correlations between the BAS GCA score and IQ measures on the WPPSI (Weschler, 1967) and WISC-III (Weschler, 1991) have been demonstrated (Elliott et al., 1996).

2.4.2 Behavioural measures

The thesis attempts to create a behavioural profile of children with RSS and compare and contrast how this differs to that seen in controls. First an overall assessment of the behaviour of children with RSS was conducted using the extended Strengths and Difficulties Questionnaire (Goodman, 1997), a widely used behavioural screening questionnaire (Goodman & Scott, 1999).

Two specific areas of behavioural disorders highlighted as potentially significant in the RSS populations are ADHD and Autistic Spectrum Disorder (ASD). While the SDQ does refer to hyperactivity in the child, it is limited, so a more in depth analysis of hyperactivity and inattention in children with RSS, relative to a control group, was conducted using the ADHD Rating Scale-IV (Home versions; DuPaul, Power, Anastopoulos & Reid, 1998). The Social Communication Questionnaire (SCQ) Lifetime edition (Rutter, Bailey & Lord, 1993) and Autism Diagnostic Observation Scale – Generic (ADOS-G; Lord et al., 1998) were used to investigate ASD in children with RSS.

2.4.2.1. Extended Strengths and Difficulties Questionnaire (E-SDQ; Goodman, 1997)

Questionnaire (Appendix L)

The SDQ is a brief behaviour screening questionnaire comprising 25 questions. The 25 items make up 5 sub-scales, measuring conduct problems, inattention and hyperactivity, emotional symptoms, peer problems and pro-social problems. Scores for the first 4 scales can be summed to give a Total Difficulties score.

The questionnaire has been designed to be completed by parents or teachers of children aged 4 – 16 years. The responses are indicated as 0, 1 or 2. A response of 0 indicates that behaviour is ‘not true’ of the child, 1, ‘somewhat true’ or 2, ‘certainly true’. Questions, 3,11,14,21 & 25 are positively worded and must be reversed in scoring. The addition of positively worded questions was done to

increase acceptability of the questionnaire to respondents, a factor not taken in to account by the Child Behaviour Check List (CBCL; Achenbach, 1991) or Rutter (Rutter, 1967) questionnaires, where all questions were negatively worded (Goodman & Scott, 1999, Goodman, 1997).

The formation of the concepts in the SDQ are based on those seen in the DSM-IV diagnostic criteria and the ICD-10, unlike the CBCL (Achenbach, 1991) and Rutter questionnaire (Rutter, 1967; Goodman & Scott, 1999). Factor analysis of the factor structure of the SDQ has repeatedly confirmed that the 5 scales create 5 independent factors (Smejde, Broman, Hetting & Von Knorring, 1999, Muris et al, 2003, Goodman, 2001).

The SDQ is available in 30 languages, indicating how widely used this scale now is. The reliability of the SDQ and agreement between scores and independent diagnosis has been established in many of the countries in which it is available, including Sweden (Smejde et al, 1999), Holland (Muris et al, 2003), Australia (Mathai et al, 2004) and Great Britain (Goodman et al, 2001, Goodman et al, 2000, Goodman & Scott, 1999). The correlation between interview based behavioural ratings and SDQ scores have been found to be better than interview ratings and CBCL scores (Goodman & Scott; 1999).

Impact supplement

The extended version of the SDQ, used here, includes a parent report impact supplement, which asks whether parents feel that their child's behaviour causes a social impairment in day to day life, in home life, friendships, classroom learning and leisure activities. The supplement comprises seven additional questions, with four possible responses, with the first two (not at all and only a little) both scoring 0, the second (Quite a lot) scoring 1 and the third (a great deal) scoring 2.

The impact supplement allows for the detection of whether or not a problem causes social impairment for the child, this is a requirement of most diagnostic criteria in DSM-IV (American Psychiatric Association, 2000) and ICD-10 (World Health Organisation) (Goodman, 1999b). Goodman (1999b) found that extending the SDQ improved the amount of information which could be taken without adding extra burden to the respondent. The impact supplement was found to be a better discriminator of cases and controls than the total symptom scores, however the best diagnosis came from using a combination of both scores (Goodman, 1999).

2.4.2.2 Attention Deficit Hyperactivity Disorder Rating Scale – IV (ADHD-IV; DuPaul, Power, Anastopoulos & Reid, 1998) (Appendix M)

The ADHD-IV is a questionnaire designed to be completed by parents (home version) or teachers (school version). There are 18 items on the questionnaire describing children's behaviours. Parents (or teacher) are asked to rate a child's behaviour, over the preceding 6 months, for each of these behaviours, on a 4 point likert scale, 0 indicating a behaviour happens 'rarely or never', to 3 indicating a behaviour has occurred 'very often'. A total behaviour score is calculated by summing all the scores given.

The questionnaire was reviewed and updated to fit with DSM-IV criteria (American Psychiatric Association, 1998) which describes ADHD as occurring in three possible forms, predominantly inattentive, predominantly hyperactive/impulsive or combined. Accordingly two factors can be taken from ADHD-IV, the total for the odd numbered questions giving a score for inattention (IA) and the total for even numbered questions a score, for hyperactivity/impulsivity (HI). This is one of the main benefits that this scale has over earlier scales such as Attention Deficit Disorder Scale (McCarney, 1989), ADHD comprehensive teacher rating scale (Ullmann, Sleator and Srpague, 1985) and Disruptive Behaviour Disorder Rating Scale (Pelham, Evans Gnagy and Greenslade, 1992), all of which were created based on earlier versions of DSM criteria (DuPaul et al, 1998). The factor structure of the questionnaire has been verified in American (DuPaul et al, 1998) and European (Dopfner et al, 2006; Zhang, Faries, vovles, Michelson, 2005) reviews of the scale.

Internal consistency of both the home and school versions of the ADHD rating scale have been found to be high for the two components (IA and HI) and total score (DuPaul et al, 1998, Dopfner et al, 2006; Zhang, 2005) and the test retest reliability was found to be high after 4 weeks for both the home and school versions (DuPaul et al, 1998, Zhang et al, 2005). A strong diagnostic and discriminate ability of the scale has also been reported (Power et al, 1998).

The most accurate prediction of ADHD presence can be achieved by using both parent and teacher rating scales (Power et al., 1998), as the two versions share a relatively low amount of variance (DuPaul et al, 1998, Cohen et al, 1990).

2.4.2.3. *Social Communication Questionnaire: Lifetime (SCQ; Rutter, Bailey & Lord, 2003)*
(Appendix N)

The SCQ (formally known as the Autism Screening Questionnaire (Berument et al, 1999), is a 40 item parent report questionnaire based on the Autism Diagnostic Interview- Revised (ADI-R, Lord et al, 1994). The ADI-R is the best validated and most widely used instrument in diagnosis of autism and related disorders, with items based on ICD-10 and DSM-IV criteria for ASD (Howlin & Karpf, 2004, Eaves, Wingert & Ho, 2006). The ADI-R and SCQ show a good correlation (0.71, $p < 0.0005$, Berument et al, 1999) and good agreement has been found between the SCQ and ADI-R in a high functioning population (Bishop & Norbury, 2002).

The SCQ is available in current and lifetime editions, the lifetime edition has been used here. This asks parents to report the presence of behaviours from 0-3 years and behaviours in the last 3 months. Question 2 asks about language ability up to the age of 3 years, if this was not present, questions 3-5 are not answered and the total score is adapted accordingly. A total score for the SCQ is calculated out of 40, additionally scores for social, communication and repetitive behaviour can be calculated, however, these have not been verified so must be used with caution (Rutter et al, 2003).

The discriminative ability of the SCQ has been found to be good (Berument et al, 1999, Eaves, Wingert & Ho, 2006), however, the cut-off score for further investigation has prompted discussion. Berument et al (1999) originally found that a cut of 15 demonstrated good sensitivity (0.96) and specificity (0.80) for discriminating a population with ASD from those with another diagnosis (not including those with intellectual impairment). This has been seen as the standard cut off since this research was conducted (Rutter et al, 1999). For this investigation a cut off of 15 was used, based on the findings of Howlin & Karpf (2004) who used the SCQ as a screening tool with a population who had a diagnosis of Cohen syndrome. In this case, most parental respondents were not attending a clinic for further investigation of ASD, as in our investigation. In this study a cut off of 15 or above on the SCQ was found to also indicate a diagnosis using the ADI-R and/or Autism Diagnostic Observation Scale (ADOS; Lord et al, 2000).

2.4.2.4 Autism Diagnostic Observation Scale (ADOS-G; Lord et al., 1998)

The ADOS-G (Lord et al., 1998) is a 30-45 minute semi-structured standardised assessment of communication, social interaction and play or imaginative use of materials conducted by a trained professional. The ADOS-G aims to elicit spontaneous behaviours of interest in the diagnosis of autism from standardized assessments with children from the age of 3 through to adulthood. The ADOS-G is made up of 4 modules, the most appropriate is chosen based on expressive language and chronological age. The behaviours observed, guide a trained professional to score the child on coding algorithms which are guided by the DSM criteria for ASD. Total scores are calculated for communication, social interaction, imagination and creativity, although only communication and interaction are used to guide diagnosis. Cut-off scores are provided for Asperger's syndrome and Autistic Disorder and while the ADOS-G is not sufficient alone to make a diagnosis of either, it has however been found to be effective in categorizing children with ASD (Lord et al., 2000; Bishop & Norbury, 2002; Bildt et al., 2004).

2.4.3 Psychosocial Measures

This thesis is attempting to look at how children with RSS compare to a control group in their body image attitude and what, if any, impact this has on their self esteem. Due to a wide age range of children recruited for this research, as a consequence of RSS being such a rare condition, two separate scales were employed to evaluate the self esteem/self concept of the children participating. It is thought that children are unable to make accurate judgements of their self worth before the age of approximately 8 years, due to cognitive limitations (Harter & Pike, 1984). To overcome this difficulty the The Pictorial Scale of Perceived Competence and Social Acceptance (Harter & Pike, 1984), was selected to assess the self concept of children under 8 years, while the Self Perception Profile for Children (Harter, 1985) was used with children over 8 years, this methodology has been used previously (Goodman, Brogan, Lynch & Fielding, 1993).

2.4.3.1 Pictorial Scale of Perceived Self Confidence and Social Acceptance for young children (PSPCSA; Harter & Pike, 1984) (Appendix O – male version)

The PSPCSA is a self report scale available in two different forms, one appropriate for use with kindergarten age children (5-6 years) and a second for use with children in grades 1 and 2 (6-8

years). The two versions of the scale are fundamentally the same and differ only on the examples used, making them more age and experience appropriate (Harter & Pike, 1984). Only the scale for use with grades 1-2 was used here.

The scale comprises 24 items, making up four sub-scales, each of six items. The sub-scales are cognitive competence, physical competence, peer acceptance and maternal acceptance. The scale takes a pictorial form, designed to not only sustain a child's attention, but also by using concrete pictures of common activities, makes it more likely to get a meaningful response from young children (Harter & Pike, 1984).

For each scale item, children are presented with two picture plates side by side, one depicts a child displaying a high level of competence or social acceptance, while the other picture shows a child with low levels of the same behaviour. The researcher asks the child which picture is most like them. Once the child has selected the picture they are asked to indicate, using the large and small circle beneath the plate, whether the picture is "a lot like them" (big circle) or "a bit like them" (small circle). A score is then given for that item dependent on the circle selected. A score of 4 is given if they select the big circle/high competence/acceptance picture down to a score of 1 for the big circle low competence/acceptance picture.

The scale was formulated using a domain specific strategy as was used by the same researchers in the development of the Self Perception Profile of Children (SPPC; Harter, 1985), though in the case of this scale it was felt inappropriate to generate a global self worth score. It was found that young children tend to choose the high scoring end of the scale (3-4), resulting in a high sub-scale mean, however standard deviations still showed variability in the scores (Harter & Pike, 1984). Reliability of the scale was found to be high ($\alpha > .80$), while sub scale reliabilities ranged from $\alpha .50-.85$ (Harter & Pike, 1984). Validity testing reported that 96% of children tested could readily give acceptable reasons for their choice of point on the scale.

The PSPCSA has been successfully used in research with groups with varying degrees of intellectual ability (Silson & Harter, 1985), language and motor abilities (Klein & Magill-Evans, 1998) and different cultures (Cain, 2000).

2.4.3.2 *Self Perception Profile for Children (SPPC; Harter, 1985) – Revision of the perceived competence scale for children (Harter, 1975; 1982) (Appendix P)*

The SPPC is a widely used measure designed for use with children from the age of 8 – 18 years to assess self confidence in different domains, in order to provide a rich, differentiated picture of their self esteem (Harter, 1985).

The scale consists of six sub-scales, each measured by 6 items. The sub-scales measure scholastic competence, social acceptance, athletic competence, physical appearance, behavioural conduct and a measure of global self worth. The sub-scales, physical appearance and behavioural conduct, are new additions to this revision of the measure (Harter, 1985).

The scale is a self report measure with each question consisting of two opposing statements, for example “some kids often forget what they learn” and “other kids can remember things easily”. Children must first select which of the two statements is most true of their usual behaviour. Once they have selected a statement, for that statement only, they indicate whether that is “sort of true of me” or “really true of me”. Questions contributing to each sub-scale are balanced through the scale and question negativity and positivity are counter balanced.

Scoring was completed by the researcher. A score of 4 was given for an item when the positive statement and “really true of me” had been selected, 3 if they selected the positive statement and “somewhat true of me, 2 for the negative statement and “somewhat true of me” and 1 for the negative statement and “really true of me”. Total scores for each sub-scale are calculated by summing responses for all questions in that sub-scale.

The scale has been found to have acceptable reliability, internal consistency and the factor structure has been confirmed across all age groups and genders for four different samples from Colorado, USA (Harter, 1985), this reliability has since been confirmed with samples in France (Boivin, vitaro & Gagnon, 1992), Holland (Van Dongen-Melma & Koot, 1993; Veerman et al., 1996), United Arab Emirates (Eapen et al., 2000), Belgium (Van den Bergh & Ranst, 1998), Ireland (Granleese & Joseph, 1992) and the US (Schumann et al., 1999). The factor structure of the scale has been found to be stable over time (Muris, Meesters & Fijen, 2003; Granleese & Joseph, 1994) and different age groups have been found to be equivalent on the scale (Van den Bergh & Ranst, 1998;

Harter, 1985). Some gender differences have been noted when using the scale, with males reporting higher competence (Van Dongen-Melman & Koot, 1993) though on the whole males and females have been found to be comparable (Granleese & Joseph, 1994; Harter, 1985; Van den Bergh & Ranst, 1998).

The SPPC has been found to display sufficient group variance in order to be used with children in clinical groups (Veerman et al., 1996), although it has also been demonstrated to differentiate within clinical groups depending on the experience of the child (Hoza et al., 1993).

The scale has previously been in used in conjunction with measures of body image attitude as it is proposed to be used in this research and was found to be an effective measure (Miller & Downey, 1999).

2.4.3.3 *Body Image Perception Attitude Scale for Children (BIPAS-C; Downey, Woodward, Pickles & Skuse, 1995)- Revised.* (Appendix Q)

Several scales have used figural drawings to establish body satisfaction and specifically weight satisfaction, though few have been tested psychometrically for reliability and validity (Gardner, 2001; Gardner, 2002; Smolak, 2004). Collins (1991) figural scale, is however an exception which has been demonstrated to have a test-retest reliability of 0.71, although the correlation between actual BMI and body image attitude rating was found to be weak. Truby & Paxton (2002) also developed the Children's Body Image Scale (CBIS) which, unlike previous scales, used digitally adapted photographs as opposed to drawings, this scale was found to be a good measure of body satisfaction and dissatisfaction, however, the pictures used were only manipulated for weight and no height equivalent was available.

For the purpose of this research the figures used in the Body Image Perception Attitude Scale for Children (BIPAS-C; Downey, Woodward, Pickles & Skuse, 1995) were used. These pictures were selected because they were available for both height and weight scales and had previously been used to assess the relationship between height and self esteem (Downey et al., 1995), however the recommend administration was revised in this research.

The BIPAS-C (1995) has two scales, height and weight. Each scale consists of five gender specific pictures, one scale increases in height from very short to very tall, while the second scale

demonstrates weight from very thin to overweight. Children are first asked which picture they think looks most like them on each scale, to follow this they are asked which they would most like to look like, with the difference between the two scores being a good indication of body shape satisfaction (Tiggemann & Pennington, 1990).

Dowdney et al (1995) recommended that the BIPAS-C be presented non-sequentially in order to avoid the effect of children responding to the socially desirable mid range, as had been found in previous research (Collins, 1991). This was found to be an effective methodology and had been replicated successfully with an Australian sample (Williams & Delin, 2001). In this research, however, it was decided to revert to previous methodology of using the pictures presented sequentially, after initial pilot testing with young children found that they were not able to discriminate the height effectively in a random presentation. In response to this finding, instructions for the study were standardised. Each child was asked to imagine that the scale depicted all the children in their class lined up, and then they were asked where would they put themselves.

In addition to using the BIPAS-C height and weight scales, a third scale was developed to assess face shape satisfaction (see appendix Q). For this, five pictures were created ranging from a face with a pointed jaw to a face with a square jaw; male and female versions were created. The methodology for using this scale was the same as that used for the height and weight scales, participants were first asked which face they thought was most like their own, they were then asked which face they would most like to have, with the difference in scores being an indication of dissatisfaction (Tiggeman & Pennington, 1990). The faces were piloted with an undergraduate sample to assess that the scale of pointed chinned to square jawed was valid.

2.4.4 Additional measures used within this thesis

In addition to the standardised measures described above all parents completed a demographic questionnaire, this was a parental report of background information including physical measurements and experiences at school and with the hospital. See appendix R for complete questionnaire.

2.5 General procedure

Once participants had returned completed consent forms, they were sent a pack of questionnaires which included the demographic questionnaire, SDQ, ADHD rating scale – IV and

SCQ. Once the completed questionnaire pack was returned, the researcher arranged a home visit with the parents. Due to the high cognitive demands of the BAS-II all participants were visited during school holidays or at weekends. During the home visit participants completed the BAS-II, the age appropriate measure of self esteem/self concept and BIAS-revised.

Following the home visit, participants were contacted again if they had scored above 15 on the SCQ, to arrange a second home visit in order to complete the ADOS-G.

2.6 Brief overview of sample and procedure in study 7

Study 7 was designed to assess how others perceived children with the physical presentation of RSS, a phenotypical facial appearance and short stature.

Participants

The study was conducted with a group of children aged 6-11 (peer group) and undergraduates at the University of Birmingham (adult group).

Peer group

The peer group was recruited through a junior school in Lancashire. Parents were sent information about the research study along with an opt-out form (see appendix S). If parents did not want their child to participate in the research at school, they returned the opt-out form to the child's teacher. Only one parent returned a completed an opt-out form. In total 143 children (71 males, 73 females), with a mean age of 6.8 years, participated (6-11 years).

Adult group

The adult group was recruited opportunistically at the University of Birmingham. Potential participants were approached by the researcher, around campus, and asked to complete a quick questionnaire. In total 120 undergraduates (59 males, 61 females) participated in the research, with a mean age of 21.05 years (18-32 years).

Procedure

The stimuli for this research was created using photographs of boys and girls aged 6-7 years. Parents and children at a school in Bedfordshire were approached to have their photographs taken for this research. In total parents of 12 children (6 boys, 6 girls) consented for their children to be photographed to create stimuli.

Full details of how the photographs taken were manipulated to create six conditions for male photographs and six for female, demonstrating manipulations in height (tall, average and short) and face shape (RSS typical and control) are given in study 7 of this thesis.

Participants, peers and adults, were to rate the version of the stimulus, with which they were presented, on physical and personality traits, using simple 1-7 likert scales. Wording of the traits was adapted between the adult and peer investigations, for example “attractive” was replaced with “good looking” in the children’s version, this was done so that wording remained age appropriate

CHAPTER 3

THE COGNITIVE PROFILE OF CHILDREN WITH RUSSELL SILVER SYNDROME (RSS)

3.1 Aims of chapter

The overall aim of this chapter was to assess the similarities in the cognitive profile of children with RSS and an age and gender matched control group.

Study 1 – A systematic review was conducted to assess the long term consequences, cognitive and behavioural, of children born SGA at term. One of the main diagnostic symptoms of RSS is that they are born SGA at term. An in-depth review of the existing literature with children with this diagnosis will be used to guide expectations and investigations through out the rest of this thesis.

Study 2 – The aim of this study was to investigate, in-depth, the cognitive abilities of children with RSS relative to an age, gender and SES matched control group. Initially differences between the RSS and control group for overall cognitive ability were assessed and following this the contributing factors to cognitive ability were investigated. Finally factors which are known to impact on SES, including birth weight, age at testing and gestational age were investigated in relation to cognitive abilities in the two groups.

STUDY 1

A SYSTEMATIC REVIEW OF THE LONG TERM CONSEQUENCES OF BEING BORN SMALL FOR GESTATIONAL AGE (SGA)

This review aims to look only at studies assessing the long term consequences of those born Small for Gestational Age (SGA) at term. When reviewing SGA literature certain considerations need to be made, the following section outlines some of the factors which were considered in this review.

3.2 Considerations made before systematic review

3.2.1 Criteria for SGA

3.2.1.1 Centile cut-off

While the standard medical practice for SGA diagnosis, using older charts, is the 10th centile, and more recent charts the 9th centile, research studies looking at the long term cognitive and psychological development of children born small for gestational age (SGA) have used a range of cut off points, from the 15th centile (Andersson, Gotlieb & Nelson, 1997; Sommerfelt et al., 2000) to the 3rd centile (O’Keeffe et al., 2003) on standardised birth weight charts. The most frequently used cut off point described in the literature is the 10th centile (Fang, 2005). A cut off point of two standard deviations below the mean expected birth weight for gestational age is alternatively used by some researchers (Bergvall, Iliadou, Johansson, Tuvemo & Cnattingius 2006; Lundgren, Cnattingius, Jonsson, & Tuvemo, 2001; Frisk, Amsel & Whyte, 2002). This is around the 2nd centile (2.25%) on older charts, and it fits exactly with the 2nd centile on the more recent UK90 growth chart.

Research into the long term consequences of those born SGA has been conducted in many different countries, all of which have used growth charts standardised on their countries populations. Care must be taken when reviewing the literature, to establish the criteria used in individual papers before generalising findings (Bos, Einspieler & Prechtel, 2001).

3.2.1.2 Birth weight or length?

Whether or not a neonate is SGA, is most commonly determined by birth weight (e.g. Hadders-Algra & Touwen, 1991; Frisk et al., 2002; Sommerfelt et al., 2000), there are incidences however where birth length (Bergvall et al., 2006; Lundgren et al., 2001) is used as an additional determinant. Research supports the idea that there is a larger effect on later cognitive abilities of small

Chapter 3: Study 1: A Systematic Review of the Long Term Consequences of Being Born Small for Gestational Age (SGA)

birth weight in a child who is below the 3rd centile for both length and weight than either alone (Lundgren et al., 2001). Birth length should however be used with caution, this is generally unreliable unless measured by specially trained professionals (Arends, Boonstra & Hokken-Koelega, 2004).

3.2.1.3 Gestational age

A confounding factor in a large number of studies is the gestational age of the children involved. Many studies look only at whether or not a child reaches the criteria for being LBW (BW<2500g), they do not differentiate between gestational ages (Taylor, Klein & Hack, 2000; Hack et al., 2002; Breslau, Paneth & Lucia, 2004). Rubin, Rosenblatt & Barlow (1973) was one of the first researchers to highlight the potential differences between a child born with a low birth weight, but appropriately sized for their gestational age and one born low birth weight but small for their gestational age. In this study, low birth weight (regardless of gestational age) was found to lead to impaired school progress, mental development, school readiness and academic achievement, however more problems were seen in the SGA low birth weight group than those appropriately sized for gestational age.

3.2.2 Recency of study

Earlier studies may be methodologically sound, controlling for the factors listed above (e.g. Rubin et al., 1973). However, findings on the long term effects of these studies have limited use today. Postnatal and prenatal care has changed extensively in the past 30 years (Wilson-Costello et al., 2007; Bhutta, Cleves, Casey, Craddock & Anand, 2002). This can be seen in the increased number of surviving children born preterm, low birth weight or very low birth weight (Bhutta et al., 2002). Detection and treatment of babies born SGA is much improved now, due to increased knowledge with prevention of adverse consequences, such as hypoglycaemia and hypothermia and this should lead to a better outcome in long term development. One of the major drawbacks therefore of research looking at the long term consequences of birth experiences is that it is not possible to predict the development of children born in the present day. Prenatal and postnatal care are constantly improving and a child born SGA assessed at 5 years will have experienced pre and postnatal care which is likely to have changed and improved in the those 5 years.

3.2.3 Exclusion criteria - Hypoglycaemia

Some studies exclude children who had experienced hypoglycaemia as neonates (Viggadel, Lundhalv, Carlsson & Kjellmar, 2004; Harvey, Prince, Bunton, Parkinson & Campbell, 1982; Walther, 1988). This is a common side effect of children born SGA. However, by excluding this group from research, the sample is not representative of children born SGA.

3.2.4 Conscription studies

Investigations, such as those by Paz et al., (2001, 1995), Lundgren et al., (2001) and Bergvall et al., (2006), allow for large groups to be compared in the countries where the research is conducted (Israel and Sweden). Both of these countries keep records of child birth weights and at the age of 17 most enter the army, completing standardised tests. The main drawback of this approach is that those with bad health will automatically be excluded from joining the armed forces. This would bias the sample, possibly away from LBW and SGA infants. In addition, as military tests are considered military secrets, knowledge of validity and reliability in some of these studies is limited (Lundgren et al., 2001).

3.3 Systematic review

Based on the above considerations, a literature search was conducted with the following restrictions. An initial search was conducted using Web of Science. The search was restricted to English language papers published between 1999 and 2007. Only studies with participants born after 1985 in Europe, North America and Australia were included. The mean GA of the samples had to exceed 36.5 weeks. Any paper which used SGA criteria of below the 15th centile or lower was included. The study could not be one which assessed the long term benefit of interventions such as growth hormone treatment or zinc. See table 3.1 for summary of literature search.

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Table 3.1: Results from systematic review literature search

Search Term		No. Articles returned by search	No. Articles meeting initial search criteria
	Psych*	110	25
Small for Gestational Age	AND		
	Cogni*	92	14
	Achiev*	108	3
	Behav*	156	7
Intra Uterine Growth Restriction/Retardation	AND		
	Psych*	24	0
	Cogni*	28	3
	Achiev*	49	1
	Behav*	64	1

(* after a term, allows for any word starting with that term to be included in the search, e.g. psych* would include **psychology**, **psychologist**, **psychiatry** etc)

A literature search was also conducted of NCBI PubMed, using the same search terms as used on WoS, this did not bring detect any additional papers to those found using WoS.

Bibliographies and citations of papers found during the literature review were also examined for further papers meeting the criteria set.

11 papers were found which adhered to the strict criteria of the literature review. Details of the studies can be seen in table 2.

Markestad et al., (1997), Andresson et al., (1997), Sommerfelt et al., (2000), Indredavik et al., (2004), Indredavik, Vik, Heyerdahl, Romundstad & Brubakk (2005) and Kulseng et al., (2006) appear to be part of a greater study into the long term consequences of being born SGA. However, the sample size and inclusion criteria of the Swedish cohort differ between studies.

Leitner et al., (2000), Leitner et al., (2007) and Fattal-Valevski et al., (1999) also appear to be conducted on the same set of participants. The sample size of these studies is almost identical. These papers will be discussed separately but as a continuation of one another.

Table 3.2: Summary of papers included in systematic review

Source and country of origin	Groups in study (inc. SGA criteria)	How were they Recruited?	Birth Weight Mean (SD) or Range	Gestational Age weeks Mean (SD)	Mean Age/Age Range at testing Weeks/Months/Years	Measures Used
O’Keeffe <i>et al</i> (2003) Australia	N=2817 Small for Gestational Age (SGA) status stratified according to BW	Subset of sample who attended antenatal clinic at regular appointments.	<3 rd % - >10 th %	>37 weeks	13.9 Years	Details of child’s school performance Questionnaire; WRT; Ravens Standard Progressive Matrices Test
Corbett <i>et al</i> (2007) UK	N=1724	Term children born April 1987-March 1988 resident in Newcastle Oct 1989	-	39 weeks	10 Years	Picture Vocabulary Test; Problems of Position Test; Reading and Math
Markestad <i>et al</i> (1997) Norway & Sweden	SGA N=260 SGA <15 th %	Recruited week 20 of pregnancy to multi-centre study, followed up at birth	3776g (26g)	+37 weeks	13 Months	Bayley Scale of Infant Development
	Average for Gestational Age (AGA) N=319	Random sample recruited at week 20 of pregnancy	2877g (15g)	+37 weeks		
Andersson <i>et al</i> (1997) Scandinavia	SGA N=142 SGA <15 th %	Invited to participate as part of the SGA Scandinavian project. Born in Trondheim or Bergen	2904g (197.2g)	39.6 (1.2)	28-41 Weeks	Fagan Test of infant Intelligence; Home Screening Questionnaire;
	AGA N=172		3745g (471.5g)	39.6 (1.2)		

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Sommerfelt <i>et al</i> (2000) Norway & Sweden	SGA N=338 SGA <15 th %	Referred to study from 3 major hospital in second trimester	<15 th %	>37 weeks	5 Years	WPPSI-R
	AGA N=335	Random 10% sample from referred population	>15 th %	>37 weeks		
Indredavik <i>et al</i> (2004) Norway	SGA N=60 SGA <10 th %	Recruited at week 20 of pregnancy to multicentre study, followed up at birth.	2921g (211g)	39.5 (1.1)	14.2 Years	KSADS; ADHD rating scale IV; ASSQ; CGAS;
	Control N=83	Random sample recruited at week 20 of pregnancy.	3691g (459g)	39.6 (1.2)	14.1 Years	
Indredavik <i>et al</i> (2005) Norway	SGA N=60 SGA <10 th %	Recruited week 20 of pregnancy to multicentre study, followed up at birth	2921g (211g)	39.5 (1.1)	14.2 Years	Child Health Questionnaire, Functional Health, Self Esteem and Well Being; Parental Bonding Instrument; Symptom Checklist; WISC III
	AGA N=83	Random sample recruited at week 20 of pregnancy	3691g (459g)	39.6 (1.2)	14.2 Years	

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Kulseng <i>et al</i> (2006) Norway	SGA N=60 SGA <10th%	Recruited at week 20 of pregnancy to multicentre study, followed up at birth.	2920g (210g)	39.5 (1.1)	14.1 Years	Knox Cube Test; Connors Continuous Performance Task; Stroop Test; Trail Making Test; Wisconsin Card Sorting.
	Control N=83	Random sample recruited at week 20 of pregnancy.	3690g (458g)	39.6 (1.2)	14.2 Years	
Fattal-Valevski <i>et al</i> (1999) Israel	SGA N=85 SGA <5 th %	All born at Lis Maternity hospital Sept 1989- Sept 1992	1860g (407g)	37.5 (2.1)	3 Years	46 item Neurodevelopmental Scale; Stanford Binet
	Controls N=85	Next born in hospital	2765g (682g)	37.6 (3.0)		
Leitner <i>et al</i> (2000) Israel	SGA N=41 SGA <5 th %	Born at Lis Maternity hospital Tel Aviv	1864g (401g)	37.6 (2.2)	6-7 Years	Detailed Neurodevelopmental exam; WPPSI
	Controls N=41	Randomly selected	2760g (763g)	37.2 (3.9)		
Leitner <i>et al</i> (2007) Israel	IUGR N=123 SGA <10 th %	Born at Lis Maternity hospital Tel Aviv	1842g (411g)	36.9 (2.6)	9-10 Years	Detailed Neurodevelopmental exam; WISC-R95; K-ABC
	Control N=63	Randomly selected.	2826g (755g)	37.6 (3.4)		

3.4 Summary of findings

This review will look at the findings of the above studies, describing the findings according to the chronological age of the samples, 28-41 weeks to 14 years.

The research studies that are reviewed mainly assess cognitive ability, that is mental ability to think, conceive and reason. Cognitive ability was usually measured using standardised tests such as the Weschler Intelligence Scale for Children (WISC) or the Fagan Test of Infant Intelligence (FTII). In addition, some researchers have also assessed neurodevelopment, this is looking at the general motor development, sensory intergration and speech and language of the children assessed.

The study with the youngest sample was conducted by Andersson et al., (1997) with children aged 28-41 weeks. This study used the generous definition of SGA <15th centile. They found that the mean cognitive score of the SGA group at this age, using the FTII, was significantly lower than that of a control group. A Home Screening Questionnaire (HSQ), which assessed the home environment, offered an alternative explanation of the effect seen. The SGA group scored significantly lower than the control group on the HSQ, indicating a worse home environment, with cognitive ability scores correlating significantly with HSQ scores. Home life in this case, was found to have a greater effect on cognitive development than birth weight status.

Markestad et al., (1997) studied a larger sample at 13 months using the Bayley Scale of Infant Development (BSID), again with the generous cut off of <15th centile. The two groups, SGA and control, did not differ at this age in their cognitive scores.

Fattal-Valevski et al., (1999), Leitner et al., (2000) & Leitner et al., (2007), conducted three separate assessments with the same population at the ages of 3 years, 6-7 years and 9-10 years. Although some drop out of the original sample was seen, this was minimal and the researchers noted that those lost at follow up did not differ significantly from those that remained in the study, at earlier assessments. These studies were unique in this review, in that they included in depth neurodevelopmental assessments.

The studies of Fattal-Valevski et al. (1999), Leitner et al., (2000) and Leitner et al., (2007) are an example of misuse of the term IUGR. Participants met strict inclusion criteria of birth weight <5th centile, although, as already discussed low birth weight alone can not be used as an indication of

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IUGR. The sample in this research can only receive a diagnosis of SGA, whether this was caused by IUGR in all cases cannot be known. Although in the original research, IUGR was used to describe the clinical sample, for this review the clinical sample will be referred to as SGA.

Fattal-Valevski et al., (1999) used the Stanford Binet (SB) test to assess cognitive ability, in children of 3 years. They did not find any difference in IQ score between the SGA and control groups, however, when further analysis took place, breaking the SGA group down in to those who did and those who did not have neonatal complications, those with neonatal complications were found to have a significantly lower IQ than those without. Despite the lack of IQ differences, the neurodevelopmental assessment of the SGA group was judged as significantly worse than controls.

This study was followed up by Leitner et al., (2000), with the same sample at 6-7 years and using the WPPSI to measure cognitive ability. Unlike the follow up at 3 years, a significant difference in cognitive scores between the SGA and control groups was found; the scores for the SGA group were, however, still within the normal range. Again the SGA group was subdivided into those with, and those without, neonatal complications. At this age, the two sub groups were not found to differ on cognitive score, similar to findings at 3 years, but the neurodevelopmental outcome of the SGA group was judged as significantly worse than controls, specifically in the areas of coordination, lateralization, spatial and graphomotor skills. Interestingly, although there was no difference between cognitive scores at 3 years, significantly more SGA children were reported as being advised to remain an extra year in kindergarten.

The most recent follow up of this sample, at the age of 9-10 years (Leitner et al., 2007) replicated the findings at 6-7 years, this time using WISC-R95 (short form), to assess cognitive ability. The SGA group scored significantly lower than the control group, but still within the normal range. At this age, academic achievement was also assessed, and it was found that the achievement of the SGA group was significantly lower than that of the control group, potentially due to a reduced number of years in education. The academic achievement assessment also highlighted a higher rate of language and speech problems at this age in the SGA group. As in both previous studies with this population, neurodevelopmental scores for the SGA group, were significantly lower than those of the

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control group. Problems were noted particularly with motor coordination, graphomotor skills and increased hyperactivity and inattention.

Sommerfelt et al., (1999) worked with children at 5 years, therefore between the ages at which Fattal-Valevski et al., (1999) and Leitner et al., (2000) conducted their research, however, for continuity, the findings from this study will be presented now. Participants in this study were born below the 15th centile and completed the WPPSI-R, cognitive ability test. It was found that the mean full cognitive score was approximately 4 points lower in the SGA group than in the control group; this difference did not reach significance. While the parents of SGA children were not found to differ significantly, for socioeconomic and cognitive factors, from those born AGA, parental factors were found to have a bigger effect on cognitive score than did SGA status.

Corbett, Drewett, Durham, Tymms & Wright (2007) worked with children at the age of 10 years, therefore overlapping with the age group assessed by Leitner et al., (2007). This study did not look specifically at SGA status at birth but the methodology highlights a different approach used with this type of research. The academic achievement of all children born at term, in one hospital in Newcastle between April 1987 and March 1988, across the whole birth weight range was assessed to look at the effects of birth weight. It was found that birth weight and cognitive outcome were weakly related, with a lower birth weight correlating with a lower cognitive score. Interestingly, this effect was maintained across the whole birth weight range and was not restricted to the low birth weight children.

O’Keeffe et al., (2003) in Australia worked with children at a mean age of 13.9 years using the WRAT and the Ravens Standard Progressive Matrices test to assess cognitive ability, as well as a report of the child’s’ school performance. The sample in this study was recruited in a similar way to Corbett et al., (2007), studying the whole birth weight range, with those below the 10th centile being defined as SGA. It was found that learning difficulties occurred significantly more often in SGA than non SGA children, with those below the 3rd centile being more severely affected than those between the 3rd and 10th centiles. This effect was found to be independent of SES. Additionally, O’Keeffe et al., (2003) looked at the attentional profile of children born SGA in comparison to controls, using the parent report Child Behaviour Check List (CBCL) and Youth Self Report Scale (YSR). While those

meeting SGA criteria did not differ on the CBCL, in terms of attention problems, SGA females, particularly those born below the 3rd centile, reported significantly more attentional problems. Males did not differ across groups.

Indredavik et al., (2004) found that with children within the SGA group studied at the age of 14 years, (SGA <15th centile), every 5th child was reported as having psychiatric symptoms, an incidence which did not differ significantly from the control group. Indredavik et al., (2005) also found that at 14 years the SGA group did not display more physical, motor or behavioural problems than controls. Self esteem and family functioning were also not significantly affected by birth weight status. Kulseng et al., (2006) looked in more depth at attentional problems in SGA children, at the age of 14 years, using tasks to assess the different components of attention. It was found that on the majority of the tasks the SGA group did not differ significantly from the control group, however, there were small significant differences between groups in tasks which required sustained attention.

3.5 What do these findings indicate?

Research suggests that there is an affect of age on the cognitive ability of children born SGA, with older children born SGA having a lower cognitive ability than controls. While Andresson et al.,'s (1997) study did find a difference in cognitive scores early in life; this could be fully explained by home life factors. Markestad et al., (1999) did not find a significant difference in scores between groups at 13 months. Fattal-Valevski et al., (1997) did not find a significant difference in cognitive scores between SGA and controls at the age of 3 years. Sommerfelt et al., (1997) did not find a significant difference between groups at the age of 5 years but did note that the mean score for the SGA was below that of the control group. Leitner et al., (2000) found that the difference in cognitive scores at the age of 6-7 years was significant, with the SGA group scoring lower than controls. This effect remained when the same sample was tested at 9-10 years (Leitner et al., 2007). The findings of Corbett et al., (2007) with a 10 year old sample and O'Keeffe et al., (2003) with a 13 year old sample, supports the idea that the deficit in cognitive abilities of the SGA group remains.

There are several potential explanations of why the cognitive abilities of children born SGA would follow this pattern, remaining comparable to controls early in life and dropping or becoming more noticeable with age.

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The neurodevelopmental findings of Fattal-Valevski et al., (1997) and Leitner et al., (2000, 2007) may offer guidance when looking at the cause of the drop in cognitive score with age. The SGA group scored significantly worse on neurodevelopmental measures than the control group when assessed at 3 years, 6-7 years and 9-10 years, although IQ did not differ at 3 years. The lower SGA neurodevelopmental scores could impact on cognitive ability in any one of three possible ways.

3.5.1 Poor neurodevelopment, leading to being kept behind in school.

Leitner et al., (2000) found, in their sample at 6-7 years, significantly more of the SGA group had been kept behind a year in kindergarten. This would have the direct effect of comparing two groups comparable in age, but not in education at 6-7 years (Leitner et al., 2000) and 9-10 years (Leitner et al., 2007). If this were the case, it may not be expected that the two groups would be cognitively comparable. However, it can be argued that as cognitive ability, rather than educational achievement, is being measured being held behind at school should have no effect. While it is known that in the sample used in Leitner et al's., 2000 and 2007 studies a proportion had been kept behind a year, it can only be inferred that there is likelihood that this has also occurred in other groups studied.

3.5.2 Poor neurodevelopmental skills leading to not being able to use school education to the best advantage

School education is geared towards being strong in certain skills, such as writing and graphomotor skills which were found to be particularly weak in the SGA group, as were speech and language abilities (Leitner et al., 2000, 2007).

Once a child is attending school, a proportion of their learning will be as part of a larger group, without the special adjustments that a parent will have made during their early years of development. If a child has a neurodevelopmental weakness such as in graphomotor skills (Leitner et al., 2000) or speech and language (Leitner et al., 2007), there is a possibility that they will not get the optimum from school based education; not developing skills in thinking, conceiving and reasoning essential components of cognitive ability. This could explain why the drop in scores occurs at an age when school has become established.

Leitner et al., (2007) also found, that at 9-10 years, attention was lower in the SGA group than in the control group, another factor which could impact on school based learning. However, studies

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which looked at behaviour specifically (O’Keeffe et al., 2003, Indredavik et al., 2004, Kulseng et al., 2006 and Indredavik et al., 2005) found few differences between the SGA and control group in problem behaviours. One drawback of these studies is that they were all conducted with children at 13-14 years; it is not known how their behaviour compared at younger ages. It is known that those born low birth weight, but not specifically SGA, have an increased incidence of attentional problems (Gray et al., 2004, Kelly et al., 2001), potentially if research were conducted with younger SGA groups, this finding would be mirrored. Interestingly, at 14 years of age, Indredavik et al., (2005) reported that physical, motor and behavioural problems in the SGA group were not greater than in controls. This may indicate that their neurodevelopment has caught up with controls and that their deficit in cognitive ability may not increase or may improve to catch up with the control group. Unfortunately, there are no data to date, that tell us what the cognitive level of those born SGA after 1985, and beyond 14 years of age is likely to be.

3.5.3 The tests used may not induce the optimal performance from the sample.

The SGA group in Fattal-Valevski et al., (1997), Leitner et al., (2000) and Leitner et al., (2007) were known to have neurodevelopmental problems, including difficulties in motor skills and language and speech. At younger ages, cognitive testing does not put as much emphasis on accuracy, spoken knowledge and speed, so these difficulties were unlikely to impact on performance at the time of cognitive testing. However, in cognitive tests designed to be conducted with older children, these skills become more important. It may be that the cognitive ability of the SGA group remains comparable to that of the control group but the method of assessing it was not suitable for this population.

3.6 Potential problems with these explanations

The three possible explanations given above for the pattern in the findings are based on the neurodevelopmental findings of one group (Fattal-Valevski et al., 1998, Leitner et al., 2000, 2007). These studies had a strict definition of SGA, <5th centile, while the other SGA groups studied had less strict criteria of the 10th centile (Kulseng et al., 2006 Indredavik et al., 2004, 2005) and the 15th centile (Andersson et al., 1997; Markestad et al., 1997; Sommerfelt et al., 2000) for SGA status. O’Keeffe et al., (2003) found that the 3rd centile could better predict IQ scores, than the 10th centile.

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Caution should therefore be taken when generalising the neurodevelopmental findings of Fattal-Valevski et al., (1997) and Leitner et al., (2000, 2007) to other populations.

While the studies of O’Keeffe et al., (2003), Indredavik et al., (2004, 2005) and Kulseng et al., (2006), give an idea of the behavioural profile of SGA children in comparison to controls at the age of 13-14 years, there is no research that describes the behavioural profile of SGA children at younger ages. It is not known whether the behaviour of SGA children differs significantly from controls during the early years of school and whether this could lead to non-optimal learning and lower cognitive scores. Leitner et al.,’s (2007) finding that attention and hyperactivity were significantly different between the SGA and control groups at the age of 10 years, may indicate that attention is a problem at younger ages and this has become less of an issue by the teenage years. Indredavik et al., (2004) stated that there was a tendency for lower behavioural scores to be observed at the age of 14 in the SGA group but that these differences were not significant.

While a review of the available literature allows an overview of the developmental course of children born SGA, there are limitations. A major difficulty with large sample data is that little is known about the early life complications of the participating individuals. Fattal-Valevski et al., (1997) and Leitner et al., (2000) compared those born SGA with and without neonatal complications and found those with complications had more cognitive and neurodevelopmental difficulties at 3 years (Fattal-Valevski et al., 1997) and 6-7 years (Leitner et al., 2000). This highlights the fact that it is difficult to take the findings pertaining to cognitive development as a whole and predict the development of all children born SGA, future research should look specifically at which risk factors are the most important in SGA long term development.

3.7 Conclusions

In summary, the number of studies which fit the strict criteria set out was limited. However, there does appear to be a pattern of lower cognitive scores in older SGA groups. This could be due to reduced neurodevelopmental skills in the SGA children, which lead to these children being held behind in school, not getting the optimum from school education or simply not being able to demonstrate their cognitive ability in the tests used. There are no comprehensive studies into the behavioural profile of SGA, term, children during the early years of school, so the impact of

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attentional problems, which have been noted in low birth weight children, but not specifically in SGA, cannot fully be taken in to account.

3.8 STUDY 2

THE COGNITIVE ABILITY OF CHILDREN WITH RUSSELL SILVER SYNDROME

Abstract

Objective: The aim of this study was to reassess the cognitive ability of children with RSS relative to an age matched control group and to investigate whether children with RSS, had difficulties in specific areas of functioning. **Method:** 23 children with RSS and 23 aged matched control children completed the BAS-II core and diagnostic scales. Children > 8 years completed the school age battery (N=17), and those > 8 years completed the early years battery (N=6). **Results:** Initial analysis compared the General Cognitive Ability (GCA) of all RSS and control children that participated, revealing a significant difference in GCA between groups. Further analysis revealed that RSS children that completed the Early Years battery did not differ significantly from controls while those that completed the School Age battery had significantly lower cognitive scores than did control children. More in depth analysis, conducted with data only from those that completed the school age battery, revealed that RSS and control groups were comparable for verbal, non-verbal and spatial ability. Within group analysis revealed that the RSS group had a significant deficit in the spatial cluster relative to the verbal cluster, however, their spatial score was significantly lower than their verbal score. Comparisons of the RSS and control children on the diagnostic scales of the BAS-II revealed some difficulties in tasks which required high levels of executive functioning. Birth weight and gestational age were both found to impact on the cognitive scores achieved by children with RSS. **Discussion:** Overall the cognitive profile found here for children with RSS, mimicked that reported in children born SGA at term. There was evidence to suggest that difficulties were increasing with age, and that difficulties were restricted to tasks with high graphomotor demands. There was evidence to suggest that cognitive difficulties that children with RSS are experiencing may be due to executive functioning problems. This area has not specifically been investigated in children born SGA at term, though there are research findings to suggest that low birth weight and gestational age, have been found to impact on both executive functioning in childhood. It is suggested that in the future a full assessment of the neurodevelopment and executive function of children with RSS should be conducted.

The Cognitive Ability of Children with Russell Silver Syndrome

Silver et al., (1953), in their initial observations of what is now known as Russell Silver Syndrome (RSS), noted that a large number of RSS children displayed learning difficulties. More recent reports of RSS state that, in the majority of cases, children and adults with RSS do not display learning difficulties and their abilities are well within a normal range (Patton, 1988; Price et al., 1999; Tanner et al., 1978; Donnai, 1989; Perkins & Hoang-Xuan 2002), though they have been found to display cognitive abilities significantly below that of age matched controls (Lai et al., 1994; Noeker & Wollmann, 2004).

Two empirical studies have assessed cognitive ability in children with RSS (Lai et al., 1994; Noeker & Wollmann, 2004). Lai et al., (1994) found that the IQ of children with RSS was on average 1SD lower than that of a control group and that they underachieved in reading and mathematics. The researchers also reported that a large number of the RSS group experienced hypoglycaemia early in life. Repeated episodes of hypoglycaemia are known to impact on a child's brain growth and development (Hume et al., 2003; Johnson, 2003) and are known to result in reduced head growth (Duvanel et al., 1997). Lai et al., (1994) found reduced head circumference, at the time of testing, in the RSS group and this was positively correlated with reduced IQ. It could therefore be hypothesised that the repeated episodes of hypoglycaemia in RSS children was responsible for the lower cognitive scores, an effect which would be reduced with more understanding of the pre and post natal complications of RSS, including hypoglycaemia.

The more recent research of Noeker & Wollmann (2004) found that although the RSS population continued to display cognitive abilities significantly below that of a control group and their siblings, the deficit was smaller than that reported by Lai et al (1994). Noeker & Wollmann (2004), unlike Lai et al (1994), did not find that head growth patterns correlated with cognitive scores. These findings suggest that the better awareness of hypoglycaemia in RSS children had reduced its incidence to the point that head growth was not compromised and was comparable to the control group. While Noeker & Wollman's (2004) findings were encouraging, they did find that children with RSS were still demonstrating a cognitive deficit, potentially due to residual levels of hypoglycaemia, or due to another unknown factor possibly linked to their Small for Gestational Age (SGA) status at birth.

Being born SGA at term, has been found to be associated with long term cognitive developmental deficits. The large scale longitudinal research of Fattal-Valevski et al (1999), Leitner et al (2000) and Leitner et al (2007), reported in the previous systematic review, offer the best overview of the cognitive development of children born SGA at more than 37 weeks, to strict criteria (<5th centile).

Fattal-Valevski et al., (1999) did not report that those born SGA were at a cognitive deficit at 3 years, though later assessments at 6-7 years (Leitner et al., 2000) and 9-10 years (Leitner et al., 2007), did report a cognitive deficit in children born SGA. At all ages an in-depth neuro-developmental assessment was conducted of children born SGA and at all stages they were found to have significant deficits, specifically in coordination, laterlaization, spatial ability and graphomotor skills (Fattal-Valevski et al., 1999; Leitner et al., 2000;2007). Overall, it was found that the SGA group's cognitive ability did not appear to be improving comparably to the control group, with increasing age. The neuro-developmental difficulties, particularly those in grapho-motor skills and motor coordination, may have been making it difficult for the SGA children to complete cognitive measures to the best of their cognitive ability. Cognitive scales used with young children put less emphasis on speed and accuracy, therefore neuro-developmental deficits, such as grapho-motor skills and poor coordination, would impact less on cognitive test scores in younger children, as was found in the research of Fattal-Valevski et al., (1999).

Study aims

- Comparison of the cognitive profile of children with RSS and an age and gender matched control group
- Assessment of impact of age, birth weight and gestational age on cognitive ability.

Method

Participants

Russell Silver Syndrome (RSS)

Parents and children aged 5-16 years with a diagnosis of Russell Silver Syndrome were recruited through the CGF. A total of 24 children with RSS were recruited to participate in this research.

Control Group

Control group participants were recruited by contacting parents and children at primary and secondary schools in Birmingham and Worcestershire and through e-mail shots in the School of Psychology at the University of Birmingham and through contacts of the researcher.

Full participant recruitment information can be found in section 2.3 Chapter 2 of this thesis, general methodology.

Table 3.3 : Group demographics

	N	Birth weight (g) <i>M (SD)</i>	Gestational Age (weeks) <i>M (SD)</i>	Test Age (Months) <i>M (SD)</i>
Russell Silver Syndrome	23 (11 male, 12 female)	1899.65 (599.69)	36.91 (3.47)	116.47 (39.51)
Control	23 (11 male, 12 female)	3487.91 (454.24)	39.52 (1.08)	116.39 (37.42)

Only those over the age of 8 years will be included in the sub-scale analysis. Those, below 8 years, who were excluded from the sub-scale analysis, did not differ significantly for birth weight or gestational age from those >8 years (see table 3.4).

Table 3.4: comparison RSS School age and RSS early years

	N	Birth weight (g) <i>M (SD)</i>	Gestational Age (months) <i>M (SD)</i>
RSS School age battery	17	1832.76 (663.38)	36.24 (3.67)
RSS Early years battery	6	2089.17 (340.33)	38.83 (2.04)
Mann-Whitney U comparison		Z=-1.191, p=.0256	Z= -1.66, p=0.117

Procedure and Measure

Each participant was visited at home either during the school holidays or at a weekend, by the researcher, where they completed the *British Ability Scale – II* (BAS-II; Elliott et al., 1996), children under 8 years completed the early years battery, while those over 8 years completed the school age battery. Details of the measure can be found in Chapter 2, general methodology, of this thesis.

Results

Kolmogorov Z tests and box plot analysis revealed that all data were normally distributed and there were no outliers, therefore parametric analysis was used throughout. While it is appreciated that using a bonferroni correction would reduce the likelihood of a type 1 error, the small sample size would increase the probability of a type II error, therefore a non corrected alpha of 0.05 will be used throughout.

Whole group GCA comparison

An independent samples t-test revealed a significant effect of group ($t=2.25$, $p=0.03$), with the mean GCA score for the RSS group (Mean= 105.43, SD=15.38), being less than the mean GCA score for the control group (Mean= 114.95, SD=12.89).

As further analysis will only be conducted with those that completed the school age battery, within group comparisons were conducted between those that completed the school age and early years battery to confirm that excluding those that completed the early years battery would not be biasing results. In addition, to further confirm this, comparisons were made between the RSS and control group for only those that completed the early years battery and only those that completed the school age battery (see table 3.5)

Table 3.5: Between group comparisons of GCA of those that completed the early years and school age batteries, and between group comparisons of only those that completed the early years battery (N=6) and school age battery (N=17).

	Early years <i>M (SD)</i>	School age <i>M (SD)</i>	Mann Whitney U comparison early years and school age
RSS	105.17 (19.07)	105.53 (14.54)	Z=0.140, p=0.92
Control	115.20 (14.95)	114.83 (13.00)	Z=-0.63, p=0.54
Mann Whitney U comparison RSS and Control	Z=1.20, p=0.33	Z=2.05, p=0.04*	

*=sig. at 0.05

Chapter 3: Study 2: The Cognitive Ability of Children with Russell Silver Syndrome

It can be seen, from table 3.5, that the GCA of the RSS and control group did not differ significantly for the early years battery only, however they were found to differ significantly for the school age battery only. It has been demonstrated that the GCA of the groups that completed the two batteries, early years and school age, did not differ significantly for either the RSS or control groups, therefore it was felt that despite there being a significant group difference for only the school age battery, excluding those that completed the early years battery from further assessment would not be biasing findings. .

Cluster Analysis

Analysis from this point forward will only be conducted with data from participants that completed the school age battery of assessments (N=17) due to the differences in the sub-scale structure of the BAS-II batteries.

Group and cluster scores were compared using a 2 x 3 split plot ANOVA. No effect of group was found ($F(1, 32)=3.76, p=0.06$), however a within participant effect of cluster was found ($F(2, 64)=7.25, p=0.002$). The interaction between cluster and group was not found to be significant ($F(2,64)=1.92, p=0.16$).

Between group analysis, using an independent sample t-test, revealed that the RSS and control groups did not differ significantly for verbal ability ($t=0.60, p=0.55$), non-verbal ability ($t=1.76, p=0.09$) or spatial ability ($t= 1.99, p=0.06$). The greatest mean difference between groups was found for spatial ability (12.06) and the smallest difference found for verbal ability (2.0).

Analysis of between cluster scores was initially conducted using a within sample t-test. The difference between scores for verbal and non-verbal ability ($t=1.66, p=0.11$) was not found to be significant. However, the difference between non-verbal and spatial ability ($t=2.17, p=0.04$) and spatial ability and verbal ability were found to be significant ($t=3.5, p=0.001$).

In order to assess that the pattern of cluster scores was true of both RSS and control groups, analysis was conducted of the two groups separately. Initially repeated measures ANOVAs were conducted which revealed a significant effect of cluster in the RSS group ($F(2,32)=7.03, p=0.004$) but not the control group ($F(2,32)=1.23, p=0.31$).

These revealed that the RSS group's spatial and verbal cluster scores differed significantly ($t=3.5$, $p=0.003$), however verbal and non-verbal ($t=2.12$, $p=0.05$) and non-verbal and spatial ($t=1.84$, $p=0.09$) clusters were not found to reach significance.

Table 3.6 shows a summary of group comparisons on all the core and diagnostic subscales of the BAS-II.

Table 3.6: Comparison of RSS and control group participants (> 8 years) on individual core scales and diagnostic scales of the BAS-II.

Scale	Russell Silver Syndrome N=17 <i>M (SD)</i>	Control N=17 <i>M (SD)</i>	t	p
Verbal core scales				
Word definitions	55.35 (6.34)	57.50 (9.49)	0.78	0.44
Verbal similarities	58.76 (5.90)	62.00 (6.79)	1.5	0.14
Non-verbal core scales				
Matrices	51.71 (11.36)	57.28 (10.66)	1.5	0.14
Quantitative reasoning	53.63 (11.22)	59.67 (6.42)	1.96	0.06
Spatial core scales				
Recall of design	47.12 (9.46)	54.28 (7.20)	2.53	0.02*
Pattern construction	50.52 (13.29)	57.78 (13.02)	1.62	0.12
Diagnostic scales				
Recall of objects immediate verbal	52.18 (12.85)	56.35 (16.78)	0.82	0.42
Recall of objects immediate spatial	47.47 (6.33)	51.62 (4.29)	2.25	0.03*
Recall of objects delayed verbal	50.88 (13.05)	54.47 (11.41)	0.86	0.4
Recall of objects delayed spatial	48.12 (6.46)	50.59 (4.70)	1.28	0.21
Speed of information processing	51.25 (9.40)	72.47 (26.38)	3.04	0.0005*
Recall of digits forward	46.65 (9.70)	55.88 (11.07)	2.59	0.01*
Recall of digits backward	48.71 (11.12)	54.59 (7.34)	1.82	0.08
Recognition of pictures	51.94 (8.83)	55.35 (7.09)	1.24	0.22

It can be seen from table 3.11 that the only core subscale for which the RSS and control group differed significantly was the recall of design. Interestingly, when the two groups were compared on the diagnostic subscales, the RSS group were also found to score significantly lower than the control

group for recall of objects immediate spatial, this along with the finding of difficulties in recall of design, and the earlier spatial cluster comparison, suggests that there is a spatial difficulty for children with RSS. The RSS group were not however found to have difficulties with the same task after a delay or Recognition of Pictures. They did score significantly lower than the control group for recall of digits forward and speed of information processing. While the difference between groups can be seen to be highly significant for speed of information processing, this may in part be due to a particularly high score for the control group children in this task.

Confounding Factors

Birth weight as a confounding factor

Birth weight has previously been found to be related to a deficit in cognitive ability (Leitner et al., 2000; Leitner et al., 2007) and a negative correlation was found here between birth weight and GCA ($r=-0.43$, $p=0.011$). The data met all assumptions to perform an ANCOVA, and this was conducted with birth weight as a covariate, this showed that when birth weight was controlled the RSS and control groups no longer differed significantly for GCA ($F(1,34)=0.209$, $p=0.651$). Therefore there is a suggestion that reduced birth weight is a significant factor in the cognitive abilities of children with RSS.

Gestational age as a confounding factor

Gestational age has previously been found to be related to lower cognitive ability (Hack et al., 2004; Indredavik et al., 2005; O'Keeffe et al., 2003; Mick et al., 2002; Elgen et al., 2004; Kelly et al., 2001) and a negative correlation was found here between gestational age and GCA ($r=0.36$, $p=0.04$). The data met all assumptions to perform an ANCOVA, and this was conducted with gestational age as a covariate, this revealed that the two groups no longer differed significantly for GCA ($F(1,34) = 1.13$, 0.29). As with birth weight therefore, gestational age alone can not be excluded as the main reason for low scores in the RSS group for GCA relative to the control group.

Discussion

The first finding of this research that is of interest, was that children that completed the early years battery of the BAS-II (<8 years) with RSS did not differ significantly for General Cognitive

Ability (GCA) from the control group. The children that completed the School Age battery were, however, found to differ significantly from the control group for GCA. This finding is of relevance as it fits with previous findings with children born SGA at term, that cognitive difficulties become more apparent with increasing age (Fattal-Valevski et al., 1999; Leitner et al., 2000; 2007). As the research of Fattal-Valevski et al. (1999) and Leitner et al. (2000; 2007) were conducted with one group longitudinally, these findings suggested that the decrease in cognitive scores were not a direct consequence of the peri-natal experience but something external such as differences in the task demands of the cognitive tests used and other factors impacting on school progression. A full review of this literature and potential consequences can be found in study 1 of this thesis.

More in-depth analysis of the cognitive profile of children with RSS was conducted with the School Age group only, due to the difference in factor structure between the Early Years and School Age batteries of the BAS-II. As already discussed, the children with RSS that completed the School Age battery differed significantly for GCA from the control group children. This reflected the findings of previous research (Lai et al., 1994; Noeker & Wollmann, 2004) that children with RSS are at a cognitive deficit relative to an age matched control group. The difference between scores here was similar to that observed by Noeker & Wollmann (2004) which was much lower than the score differences observed by Lai et al., (1994), 10 years previously. These findings can therefore be taken as further support that any cognitive difficulties observed in children with RSS are not as significant as initial research indicated.

A comparison of the RSS and control group scores on the three sub-tests which contribute to the GCA, verbal ability, non-verbal ability and spatial ability, revealed no significant group differences. It was observed that the RSS group were scoring lower than the control group in all domains, with the largest between group difference seen in the spatial index.

Within group across index analysis revealed on a significant difference between indexes for the RSS group with post hoc analysis showing that verbal ability was significantly better than spatial ability and while non-verbal ability was not also significantly better than spatial ability this was approaching significance. This finding is important and fits in some ways with previous research with children born SGA at term. The spatial components of the BAS require good hand eye coordination,

fine motor skills and grapho-motor control (Elliott et al., 1996). SGA children born at term, have at all ages been found to have significant neuro-developmental difficulties, specifically grapho-motor skills and motor coordination (Fattal-Valevski et al., 1999; Leitner et al., 2000;2007). Analysis of the individual sub-tests which make up the different indexes of the BAS-II revealed that the only core sub-test which the two groups differed significantly for was the 'Recall of Designs', this task is very dependent of good fine motor skills and accuracy, while the second spatial task, 'Block Design', is less so. This finding adds further support to the argument that the difficulties that children with RSS are perceived to have are due to fine motor skills difficulties, this is an area that would need further directed investigation.

While the explanation given above for the lower spatial abilities in children with RSS is plausible, the between group comparisons on the supplementary items of the BAS-II provide an alternative further explanation for the difficulties the RSS children were having on the Recall of Design task. RSS children scored significantly lower on the immediate spatial recall task, recall of digits forwards task and speed of information processing task, all tasks, along with the Recall of Design task, require executive functioning. Executive functions are self regulatory neuro-cognitive processes that include the ability to inhibit, shift set, plan, organize, use working memory, problem solve and to maintain a set in order to attain future goals (Willcutt, Doyle, Nigg, Faraone & Pennington, 2005; Seidman, 2006). There is no research which specifically assesses executive functioning in children born SGA at term, though there is a body of research which assesses these factors in extreme low birth weight, and premature groups. These suggest that not only visual-motor skills, as has been documented in children born SGA, but also memory and executive functioning are the most affected areas of cognitive functioning as a consequence of reduced birth weight and gestational age (Taylor et al., 2004; Woodward et al., 2005). The fact that peri-natal factors have previously been associated with executive function difficulties, in combination with the findings from this research that children with RSS have difficulties with tasks which rely on executive function, presents the case that further research should be conducted to assess executive function in children with RSS. It is particularly important to find whether specific areas of executive function are impacted, this would offer opportunities for intervention with the most at risk children.

The final finding from this study was that when birth weight and gestational age were both independently controlled for, the differences in GCA scores between the RSS and control groups were no longer significant. This finding adds further support to the arguments above based on the findings with children without RSS, born low birth weight, prematurely and SGA at term. Any effects on cognitive ability seen in children with RSS are directly correlated to their degree of peri-natal compromise. This is an important finding, and has some real life application. RSS children with higher birth weights and gestational ages are less likely to encounter difficulties with their cognitive profile.

Summary

This research replicates the findings of Noeker & Wollmann (2004) with children with RSS, which found that they have a cognitive deficit relative to an age matched control group, this was however found to be true only on those children over 8 years in this research. This finding fits with previous findings with children born SGA at term, in that younger SGA children do not have difficulties on cognitive assessments though differences became apparent with age. The reason for differences could be predicted to be due to the different task demands for older children in cognitive assessment. Further findings indicated that RSS children were having difficulties with tasks with high grapho-motor skill demands, and executive functioning demands, further investigation of these areas of functioning are recommended as both areas have previously been highlighted as areas of difficulties in children with aversive peri-natal consequences, and in this research birth weight and gestational age could be seen to be significantly important in overall cognitive ability scores.

3.8 Chapter 3: Discussion

The aim of this chapter was to assess the cognitive development of children with RSS in comparison to a control group.

Study 1, a systematic review of the long term consequences of children born SGA at term, was conducted as one of the main features of RSS is being born SGA at term. It was hypothesised that there would be similarities in the cognitive and behavioural development of children with RSS and SGA and this could guide the hypotheses made in study 2 and chapter 4 of this thesis.

The systematic review revealed that children born SGA at term develop cognitive difficulties through their lives. Studies at early ages (3 years) did not reveal a cognitive deficit in SGA children relative to controls, however, cognitive deficits tended to be detected at later ages. At all ages, a neuro-developmental deficit was found in children born SGA, specifically in fine motor, hand eye coordination, and grapho-motor skills. It could therefore be hypothesised that the difficulties seen in older SGA children were as a consequence of their neurodevelopmental difficulties making it difficult for them to achieve high scores in testing, as more reliance on these skills is put on cognitive testing at an older age than at younger ages.

Study 2 investigated the cognitive profile of children with RSS. This study revealed that overall the RSS group were at a cognitive disadvantage relative to the age matched control group, though this was only true of the RSS children that completed the School Age battery. The RSS group were not found to differ from the control group for verbal, non-verbal or spatial ability, however, they were found to display a significant deficit in the spatial cluster relative to the verbal cluster. This finding adds support to the hypothesis that children with RSS have a similar cognitive profile to children born SGA, with any cognitive difficulties seen being due to being born SGA, rather than RSS as a syndrome. Here RSS children were displaying difficulties in the tasks with the highest demand for grapho-motor skills, and motor control, both of which SGA children had been found in study 1 to have difficulties with. It was alternatively hypothesised that the difficulties the RSS children were experiencing could be as a result of executive functioning difficulties, rather than motor difficulties. When both birth weight and gestational age were controlled for, it was found that the difference in

cognitive ability between the two groups reduced and was no longer significant. Overall the findings from this research study suggest that any cognitive difficulties that children with RSS are encountering appear to be due to their peri-natal experiences, rather than a direct consequence of RSS as a syndrome. This is a largely encouraging finding, it suggests that those RSS children most at risk of cognitive difficulties can more easily be detected early in life, with an increased awareness leading to better detection and intervention for difficulties. What this research can not conclusively do, is explain what the exact difficulties they are likely to encounter are, although it can suggest that the difficulties are either due to fine motor difficulties or executive functioning difficulties, this needs further investigation.

The aim of the following chapter is to further investigate the behavioural profile of children with RSS. As in study 2 of this chapter, the findings from study 1, the systematic review, will be used to guide the research hypothesis and findings.

CHAPTER 4

THE BEHAVIOURAL PROFILE OF CHILDREN WITH RUSSELL SILVER SYNDROME

4.1 Overview of chapter

The aim of this chapter was to create a behavioural profile of children with RSS, this was further to parental and physician reports of increased behavioural problems, specifically increased incidence of Attention Deficit Hyperactivity Disorder (ADHD) and Autistic Spectrum Disorder (ASD).

Study 3 – The aim of this study was to create a behavioural profile of children with RSS relative to an age, gender and SES matched control group. Initially a screening questionnaire, the Strength and Difficulties Questionnaire (Goodman, 1997) was used to compare RSS and control behavioural profiles. Following the findings of this comparison, hyperactivity and inattention was further investigated. Factors which have previously been found to impact on behavioural difficulties, including birth weight and gestational age, were investigated to ascertain whether these alone could account for the difference in cognitive profile between RSS and control groups.

Study 4 - The aim of this study was to investigate the incidence of ASD in children with RSS. The Social Communication Questionnaire (Rutter, Bailey & Lord, 2003) was used to screen both RSS and age and gender matched control children, for social and communication difficulties. Following findings from the screen, all children that reached a cut-off for further investigation were followed up using the Autism Diagnostic Observation Schedule (Lord et al., 1998). A comparison was made of those children with RSS that met ASD criteria on both measures, and those that did not meet criteria to look for differences in birth weight, gestational age, symptom presentation, treatment and other factors.

4.2 STUDY 3

THE INCIDENCE AND DESCRIPTION OF BEHAVIOURAL PROBLEMS AND ADHD IN CHILDREN WITH RUSSELL SILVER SYNDROME (RSS)

Abstract

Objective: This study was conducted to investigate the behavioural profile of children with RSS further to parental and physician reports of increased behavioural difficulties. Particular attention was paid to the increased incidence of ADHD symptoms. **Method:** The parents of twenty four children with RSS and twenty four age matched controls completed the ESDQ (Goodman, 1997) ADHD-Rating scale IV (DuPaul et al., 1998). Between group comparisons were made for scores on the scales, and further analysis was conducted to assess for possible causes of the raised scores in the RSS group. **Results:** As a whole group, the RSS group parents reported significantly more behavioural difficulties than did control parents. RSS parents were also found to report significantly more ADHD symptoms, on both hyperactivity/impulsivity and inattention sub-scales of the ADHD rating scale-IV. Gender analysis revealed that RSS males reported significantly more symptoms of hyperactivity/impulsivity and inattention, while RSS females reported only significantly more symptoms of inattention. Controlling for birth weight and gestational age did not reduce the difference between RSS and control groups for ADHD symptoms, and cognitive ability was not found to correlate significantly with ADHD symptoms in children with RSS. **Discussion:** Children with RSS were found to display significantly more behavioural difficulties than an age matched control group, and further investigations showed significantly more symptoms of ADHD. Birth weight and gestational age alone could not account for the increased levels of ADHD in the RSS group, and it is thought that post-natal complications play a significant role in increasing ADHD levels, though this needs further investigation.

The Incidence and Description of Behavioural Problems and ADHD in Children with Russell Silver Syndrome (RSS)

There is little known about the behavioural profile of children with RSS although anecdotal reports have implied that there is a raised level of behavioural problems. The only published research to date, a meeting abstract, assessed ADHD in children with RSS (Bogdanov, Menassepalmer, Lesser, Levy & Marion, 1995) and found a higher than expected ADHD incidence.

One of the main symptoms of RSS is being born Small for Gestational Age (SGA) at around term. While low birth weight has been found to be a risk factor for increased behavioural difficulties (Hack et al., 2004; Indredavik et al., 2005; O'Keeffe et al., 2003; Mick et al., 2002; Elgen et al., 2004; Kelly et al., 2001) being born SGA at term has not been found to be a significant risk factor for behavioural difficulties (O'Keeffe et al., 2003; Indredavik et al., 2003; Indredavik et al., 2005). It has been found, however, that children born SGA with post-natal complications report significantly more symptoms of ADHD, while those without complications did not differ significantly from controls (Robson & Cline, 1998). Children with RSS are at risk of post-natal complications, such as hypoglycaemia and hypothermia due to their feeding difficulties, and poor weight gain, and therefore may be at an increased risk of developing ADHD.

ADHD background

Attention Deficit Hyperactivity Disorder (ADHD) is a disorder characterized by developmentally inappropriate levels of inattention and hyperactivity (American Psychiatric Association, 2000). Estimates of the incidence of ADHD in school age populations range from 5-16% (Faraone et al., 2003; Biederman & Faraone, 2005; Wolarich et al, 1998) with the male to female ratio for ADHD reported as between 3:1 and 9:1 (Swanson et al., 1998; Milich et al., 2001)

There are reported gender differences in children with ADHD. Girls with ADHD have been found to display less disruptive behaviours and more internalizing problems, than do boys (Biederman, 2002; Levy, 2005), with males more often referred to clinical services than females due, in part, to the greater degree of externalizing and rule breaking behaviours that they display (Biederman 2002; Levy et al., 2005).

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Those with ADHD are known to be at an increased risk of having social difficulties in childhood and are often the last children chosen as play partners (Holowenko, 1999; Biederman, 2005). Children with a diagnosis of ADHD are also at high risk of academic failure due to difficulties maintaining attention in class-room situations (Biederman, 2005). In adulthood, ADHD has been associated with increased delinquency, peer rejection, externalising anti-social disorders and substance abuse (Biederman, 2005; Murphy et al., 2002). These potential consequences highlight the importance in recognising, as early as possible, whether or not a child is at risk of ADHD.

What causes ADHD?

While there is a strong genetic indication in ADHD (Faraone & Biederman, 1998; Milichap, 2008; Cantwell, 1975; Morrison & Steward, 1973) it is believed to be multi-factorial with environmental factors, such as lead exposure (Gittelman & Eskenazi, 1983; Nigg et al., 1998), maternal smoking (Mick et al., 2002; Button et al., 2007), complications at birth (Faraone & Biederman, 1998; Milberger et al., 1997; Sprich-Buckminster et al., 1993) and low birth weight (Hack et al., 2004; Indredavik et al., 2005; O’Keeffe et al., 2003; Mick et al., 2002b; Elgen et al., 2004; Kelly et al., 2001) all being important. Events that result in a reduced oxygen supply to the fetus/neonate for a prolonged period are more likely to be associated with an increased level of ADHD (Faraone & Biederman, 1998; Biederman & Faraone, 2005), possibly as a consequence of selective neuronal damage (Swanson et al., 1998).

The aim of the current study is first to provide an overview of the behavioural profile of children with RSS relative to that of an age matched control group. It is hypothesised that RSS children will display significantly more behavioural problems than do the control group, with the difficulties being restricted to ADHD symptoms. Further to the overview a more in depth analysis will be conducted of ADHD symptoms in children with RSS, with the prediction that they will display significantly more ADHD symptoms, than do the control group. It is hypothesised that there will be some gender differences in the incidence of behavioural problems, with RSS males displaying more externalising behaviours relative to the control males, than RSS females.

Study aims

- Comparison of the behavioural profile of RSS children with a gender and age matched control group.
- A more in-depth investigation of the symptoms of ADHD in children with RSS in comparison to an age matched control group, with emphasis on gender differences.
- Assessment of the impact of age, birth weight and gestational age on behavioural profile.

Method

Participants

Russell Silver Syndrome (RSS)

Parents and children aged 5-16 years with a diagnosis of Russell Silver Syndrome were recruited through the CGF. A total of 24 children with RSS were recruited to participate in this research.

Control Group

Control group participants were recruited by contacting parents and children at primary and secondary schools in Birmingham and Worcestershire and through e-mail shots in the School of Psychology at the University of Birmingham and through contacts of the researcher.

Full details of recruitment of participants can be found in section 2.3, chapter 2 of this thesis, general methodology.

Table 4.1: Demographics of Russell Silver Syndrome group and Control group

	N	Birth weight (g) <i>M (SD)</i>	Gestational Age (weeks) <i>M (SD)</i>	Test Age (months) <i>M (SD)</i>
Russell Silver Syndrome (RSS)	24 (12 male, 12 female)	1920.50 (595.33)	37.04 (3.46)	117.00 (38.72)
Control	24 (12 male, 12 female)	3496.00 (446.01)	39.54 (1.06)	116.63 (36.62)

Measures and procedure

All parents of children participating in this research completed the Extended Strength and Difficulties Questionnaire (ESDQ; Goodman, 1997) and the Attention Deficit Hyperactivity Disorder Rating Scale-IV Home version (ADHD-IV; DuPaul et al., 1998). Questionnaire measures were sent to

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parents to complete and returned to the researcher. All children also completed the BAS-II (Elliott et al., 1998; full results from this measure are reported in Study 3 of this thesis). Full details of the measures used here can be found in Chapter 2 of this thesis, general methodology.

Results

Kolmogorov Smirnov Z tests revealed that the data was normally distributed and box plot analysis did not reveal any outliers, therefore parametric analysis has been used throughout. Due to the number of comparisons to be made, it would be advisable to use a conservative, bon ferroni corrected alpha to reduce the chance of type 1 errors, however, due to small sample size this would increase the probability of type 2 errors. It was therefore decided to use an alpha of 0.05 throughout.

Extended Strengths and Difficulties Questionnaire (ESDQ; Goodman, 1997).

Whole group comparison

A two factor (group and gender) multivariate analysis of variance (MANOVA) was conducted to determine whether RSS children displayed more behavioural problems than control group children and to assess for gender differences. Because the user guidelines for the SDQ (Goodman, 1997) state that the Total Difficulties calculation should not include scores from the Pro-Social sub-scale, therefore this was excluded from the MANOVA. The multivariate tests for group was found to be significant ($F(4, 39)=4.97, p=0.002$) although the multivariate test for gender was not found to be significant ($F(4, 39)=2.37, p=0.07$). The interaction between group and gender was not found to be significant ($F(4, 39)=1.95, p=0.12$). Univariate analysis, revealed that the RSS group reported significantly more emotional difficulties ($F(1,46)=5.21, p=0.03$), conduct problems ($F(1,46)=5.41, p=0.03$), peer problems ($F(1,46)=6.22, p=0.02$) and hyperactivity ($F(1,46)=18.62, p=0.000$) than did the control group.

Males

A one factor, group (RSS or Control) MANOVA was conducted, comparing RSS and control males only and this was found to be significant ($F(4,19)=4.20, p=0.02$). Univariate analysis revealed significant group differences for Hyperactivity ($F(4,19)=14.61, p=0.001$) and Peer Problems ($F(4,19)=5.36, p=0.03$) (see table 4.2 for full output).

Females

A one factor, group (RSS or control) MANOVA was conducted, comparing RSS and control females only, this was not found to be significant ($F(4,19)=2.39$, $p=0.09$). Univariate analysis only revealed a significant group difference for emotional problems ($F(4,19)=7.02$, $p=0.02$) (see table 4.2 for full output).

Table 4.2: Univariate analysis comparison of RSS males (N=12) and control males (N=12) and RSS females (N=12) and control females (N=12) group for SDQ subscale and total score.

	Male RSS <i>M (SD)</i> N=12	Male Control <i>M (SD)</i> N=12	MANOVA		Female RSS <i>M (SD)</i> N=12	Female Control <i>M (SD)</i> N=12	MANOVA	
			F	p			F	p
Emotional	4.00 (2.86)	1.25 (2.18)	0.27	0.61	2.50 (2.65)	1.67 (1.32)	7.02	0.02*
Conduct	1.83 (1.7)	0.92 (1.78)	4.08	0.06	2.0 (2.0)	0.56 (1.01)	1.67	0.21
Hyperactivity	4.5 (2.84)	1.75 (2.34)	14.61	0.001*	5.92 (2.03)	2.44 (1.42)	6.69	0.17
Peer Problems	2.0 (2.17)	1.25 (1.37)	5.36	0.03*	3.92 (2.23)	1.0 (1.66)	1.03	0.32

*= $p<0.05$

Impact Supplement

Parental reports from the impact supplement of the SDQ were converted to band scores according to the guidelines set out by Goodman et al., (1997). Those with a score of 0 were rated as 'no reported problem', a score of 1-2, 'possible behavioural problem' and a score of 2+, 'a definite behavioural problem'. A chi square analysis was then conducted comparing the RSS group and control group.

This showed a significant group difference ($\chi^2=0.93$, $p<0.001$) with RSS parents reporting definite behavioural problems more than control parents (see table 4.3). A further analysis was conducted splitting the groups by gender, these revealed that for neither the males ($\chi^2=4.52$, $p=0.10$) or females ($\chi^2=5.14$, $p=0.07$), were the RSS parents found to report more definite behavioural problems than control parents (see table 4.4).

Chapter 4: Study 3: The Incidence and Description of Behavioural Problems and ADHD in Children with Russell Silver Syndrome (RSS)

Table 4.3: Chi square comparison of RSS (N=24) and control (N=24) whole group for SDQ impact supplement.

	Definite problem	Possible Problem	No Problem
RSS	12	2	10
Control	5	0	19
Chi-square	Chi=0.933, p<0.01*		

*=p<0.01

Table 4.4: Chi square comparison of RSS males (N=12) and control males (N=12) and of RSS females (N=12) and control females (N=12) for SDQ impact supplement

	Male			Female		
	Definite	Possible	No	Definite	Possible	NO
RSS	7	1	4	5	1	6
Control	3	0	9	1	0	11
Chi square	Chi=4.52, p=0.104			Chi=5.14, p=0.07		

ADHD Rating Scale – IV (DuPaul et al., 1998).

The data from the ADHD rating scale-IV was analysed using a two factor MANOVA (RSS or Control; male or female). The analysis revealed there was a multivariate difference between the two groups, RSS and Control, that was unlikely to be due to sampling error ($F(2,45)=10.78$, $p<0.001$), however no effect of gender was detected ($F(2,45)=0.52$, $p=0.60$).

Univariate analysis was conducted to compare RSS and control groups on the two contributing DVs (inattention and hyperactivity/impulsivity). The univariate analysis revealed a significant effect of group for inattention ($F(2,45)=21.96$, $p<0.001$) and hyperactivity/impulsivity ($F(2,45)=11.12$, $p=0.002$).

Although no effect of gender was found in the above analysis, this only reveals that overall males and females did not differ significantly for inattention and hyperactivity combined. Further analysis is necessary to assess for the simple effects for males and females separately.

Male

The male only data was analysed with a one factor MANOVA (RSS or Control). The analysis revealed a multivariate difference between the two groups, RSS and Control, that was unlikely to be due to a sampling error ($F(2, 21)=7.20$, $p=0.005$). The analysis revealed a significant effect of group for inattention ($F(1,22)=14.01$, $p=0.001$) and hyperactivity/impulsivity ($F(1,22)=9.03$, $p=0.007$).

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Female

The female only data was analysed with a one factor MANOVA (RSS or Control). The analysis revealed there was a multivariate difference between the two groups, RSS and Control, that was unlikely to be due to a sampling error ($F(2,21)=3.79$, $p=0.04$). Univariate analysis, revealed a significant effect of group for inattention ($F(1,22)=7.89$, $p=0.01$) but not for hyperactivity/impulsivity ($F(1,22)=2.72$, $p=0.12$).

Age as a confounding factor

It has previously been shown that ADHD symptoms can decrease with age (DuPaul et al., 1998). To this point in the analysis, age of participants has been controlled by age matching RSS and control participants. However, before further analysis is carried out, an effect of age needed to be assessed for, as this may need to be controlled for. Correlations were conducted between total difficulties and age ($r=0.027$). The correlations were found to be weak, therefore any effects reported from this point are not likely to be confounded by the age of the child, and the age of the child does not need to be controlled statistically.

Birth weight

Birth weight has previously been found to be related to an increased incidence of ADHD symptomology (Hack et al., 2004; Indredavik et al., 2005; O'Keeffe et al., 2003; Mick et al., 2002; Elgen et al., 2004; Kelly et al., 2001) and a negative correlation was found here between birth weight and total ADHD difficulties ($r=-0.44$, $p=0.002$). The data met all assumptions to perform an ANCOVA, and this was conducted with birth weight as a covariate, this showed that there was still a significant difference between groups for total ADHD difficulties ($F(1,45)=7.93$, $p=0.007$). It can therefore be confirmed that birth-weight cannot account for the increased ADHD difficulties found in the RSS group.

Gestational Age

Gestational age has previously been found to be related to an increased incidence of ADHD (Lou, 1996). A significant negative correlation was found here between gestational age and total ADHD difficulties ($r=-0.33$, $p=0.02$). The data met all assumptions to perform an ANCOVA, and was conducted with gestational age as a covariate, this revealed that even when gestational age was

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controlled there was a significant group difference for total ADHD difficulties ($F(1,45)=12.73$, $p=0.001$). This finding suggests that gestational age can not account for the increased ADHD difficulties found in children with RSS.

ADHD level and cognitive ability

ADHD is known to be associated with an increased level of academic failure as a consequence of lack of attention in classroom situations (Biederman, 2005) and this in turn could impact on performance in cognitive testing. A very weak, non-significant, correlation was found between General Cognitive Ability (GCA), from the BAS-II (results reported previously in Study 2 of this thesis) and ADHD total difficulties ($r=-0.35$), which suggests that cognitive ability is not being impacted in the RSS group by an increased level of ADHD symptomology. Further correlations were conducted between ADHD total difficulties and verbal ability ($r=0.122$), non-verbal ability ($r=-0.073$) and spatial ability ($r=-0.078$), again ADHD difficulties were not found to correlate with a specific area of cognitive functioning.

Discussion

A comparison of the behavioural profile of children born RSS and an age matched control group revealed a significantly increased incidence of, parentally reported, Total Behavioural Difficulties in the RSS group. Sub-scale analysis revealed that the two groups differed significantly for reported hyperactivity, emotional problems, conduct problems and peer problems, with parents of RSS children reporting more symptoms of all problem behaviours than did control group parents. It was also found, using the SDQ impact supplement, that significantly more parents of RSS children felt their children had definite behavioural difficulties than did parents of control group children. As there are currently only anecdotal reports of increased behavioural problems in children with RSS, it is unlikely that these findings reflect response bias, though there does remain the possibility that RSS children with the most behavioural problems, are more likely to have participated in this research.

Overall, males and females were not found to differ significantly for behavioural problems, however, further analysis conducted compared RSS and control males and RSS and control females. For males, a significant between group difference was found for behavioural difficulties, though,

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univariate analysis revealed that the two groups only differed significantly for reported peer problems and hyperactivity. The RSS females, however, were not found to differ significantly from the control group, for total behavioural difficulties, though they were found to display more emotional problems than were control children.

Females, in general, have been found to display fewer externalising behaviours of hyperactivity, and this may be why ADHD is less diagnosed in females than males (Biederman et al., 2002; Levy et al., 2005). As the initial questionnaire used here, the SDQ, was only very brief with 5 questions assessing the diverse concept of inattention and hyperactivity, it was important to assess both the hyperactivity/impulsivity and inattention components of ADHD in males and females with the more extensive questionnaire, the ADHD rating scale -IV (DuPaul et al., 1998). This revealed, as expected, that both RSS males and RSS females were reporting more symptoms of ADHD than control groups, however, in females this was limited to more symptoms of inattention, while males displayed more hyperactivity/impulsivity and inattention.

When divided according to gender, neither parents of RSS males nor females reported behavioural difficulties which significantly impacted on their day to day life to a greater extent than was reported by control group parents. This was despite the fact that, as a whole group, parents reported that they felt that children with RSS were significantly more disadvantaged. This finding suggests that there is no gender bias in how parents perceive the influence of behavioural difficulties; which is surprising. RSS males were found to display more hyperactivity than the control males, an externalising behaviour, which is usually associated with an increased referral bias because the problems are seen as a cause for concern. It was therefore expected that parents of RSS males would report significantly more impact of behavioural difficulties on day to day life, however this was not found to be the case.

Further investigations of the ADHD reported here in children with RSS, revealed that birth weight, reduced gestational age and, in turn, degree of prenatal growth compromise, were found to be significantly correlated with total ADHD score, however when the RSS and control group total ADHD scores were again compared, while statistically controlling for birth weight or gestational age, they continued to differ significantly. Low birth weight alone therefore can not be the cause of the

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increased ADHD seen in the RSS children here. This was largely as expected, as previous research with children born SGA at term, failed to find a direct link between birth weight at term and increased attention difficulties (Indredavik et al., 2005; 2003). What was found to be critical, however, was the immediate postnatal experience (Robson & Cline, 1998), specifically reduced oxygen and nutrient supply for a prolonged period (Faraone & Biederman, 1998; Biederman & Faraone, 2005), have been found to be more important in the development of ADHD. While children with RSS are generally born at term, they, as part of the syndrome, nearly always report early life complications particularly in feeding which is evidenced by the fact that they are often tube fed immediately post-natally to counter their poor feeding. Poor weight gain puts children with RSS at an increased risk of post-natal complications. The complications that they experience, however, differ from child to child, with birth weight not being a direct indication of the complications they will experience; post natal complications rather than birth weight may be a better indication of expected ADHD in RSS children.

In this research, the cognitive abilities of children with RSS were not found to correlate with the parentally reported incidence of ADHD symptoms. It may have been expected that increased ADHD symptoms would have been associated with decreased cognitive ability as evidence suggests that ADHD can cause reduced concentration in class with an overall deficit to cognitive abilities (Biederman, 2005). Cognitive ability may not however have been the appropriate measure to assess whether ADHD levels were having a significant impact on the child's development, academic achievement may have been more appropriate. Equally, in this research only parental reports of ADHD have been used, this is a weakness in the methodology as it has been found that the best reports of children's ADHD level would be when both parents (home) and teacher (school) ratings were combined (DuPaul et al., 1998). Findings here can only be taken to describe home experience, and it can not be ruled out that school behaviour is significantly different for the child and this would be the most relevant to their cognitive and academic development.

45-94% of those with Attention Deficit Hyperactivity Disorder (ADHD) have been found to manifest more emotional, personal, family and interpersonal functioning problems than do controls (Biederman, 2005; Hurtig, 2007). It can be hypothesised that the significant increase in peer problems

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in males with RSS and emotional problems in females, may be secondary to their increased difficulties caused by reduced attention and increased hyperactivity.

Summary

The most significant behavioural difficulty reported in children with RSS was hyperactivity/inattention, although other behavioural difficulties were detected, these may be secondary to increased symptoms of ADHD (Biederman, 2005; Murphy et al., 2002).

While both males and females were found to report significantly more symptoms of ADHD, there were, as expected, some gender differences. While males reported more symptoms of hyperactivity/impulsivity and inattention, RSS females were only found to report significantly more inattention, an internalising behaviour.

Low birth weight and reduced gestational age were found to be significantly related to the increased incidence of ADHD in children with RSS, however, when this was controlled for the RSS children were still found to display significantly more symptoms of ADHD. What could not be controlled for in this study, and may be critical, is the post natal complications experienced by the participating children with RSS.

Finally, reported ADHD symptoms were not found to correlate with the general cognitive ability of children with RSS, this suggests that ADHD symptoms are not having a direct impact on cognitive ability, though this may be due to an inappropriate measure, or the use of only parental reports of ADHD, and not teacher reports.

Overall, the findings of this research are that children with RSS are at an increased risk of ADHD, not as a consequence of birth weight or reduced gestational age, although post-natal complications may be critical.

4.3 STUDY 4

AUTISTIC SPECTRUM DISORDER AND RUSSELL SILVER SYNDROME (RSS): INCIDENCE AND RISK FACTORS

Abstract

Objective: Parents and physicians have anecdotally reported a raised incidence of ASD in children with RSS. This research aimed to estimate the incidence of ASD in RSS and, further to this, to assess whether those with RSS and ASD formed a homogenous group. **Method:** Parents of children with a diagnosis of RSS completed the SCQ screening questionnaire, those who scored <15 on this were followed up using the ADOS-G as a further indicator of ASD. Those with RSS that met ASD criteria on both measures were then compared on a number of demographics with those with RSS without ASD. **Results:** A sub-group of four children were found to have RSS and to meet ASD criteria, estimating the incidence of ASD in RSS to be approximately 1.6 in 10. Those with ASD-RSS were not found to differ significantly from the rest of the group on any demographic factors. **Discussion:** The incidence of ASD is raised in children with RSS. Those with RSS and ASD could not be differentiated from those with RSS without ASD for RSS symptom presentation or pre-natal or birth factors. It is hypothesised that those with RSS-ASD would have displayed the milder ASD phenotype, often seen in relatives of children with diagnosed ASD, but RSS is acting as a trigger for this to become diagnosable ASD.

Autistic Spectrum Disorder and Russell Silver Syndrome: Incidence and Risk Factors

The incidence of Autistic Spectrum Disorder (ASD), specifically Asperger's syndrome, in children with a diagnosis of RSS has anecdotally been reported by physicians to be higher than expected in the general population. This research aimed to explore first of all whether the incidence of ASD was raised in comparison to the expected rate in the general population and further to look for potential clues as to why this is the case.

A recent estimate of the incidence of ASD in the general population is 6.7 in every 1000 people (Centre for Disease Control and Prevention in the US, 2007). There is known to be a large genetic component to the incidence of ASD, with a higher concordance in monozygotic twins than dizygotic twins (Bailey et al., 1995) and high sibling incidence (Gillberg & Coleman, 2000; Chakrabarti & Fombonne, 2001; Spence, 2004; Zhao et al., 2007). The inheritance of ASD is not simple, and there are thought to be up to 15 genes involved (Risch et al., 1999) with the broader ASD phenotype seen in 1 in 5 relatives of children with ASD (Rutter, 2005) resulting from only a proportion of the genes being abnormal in these relatives.

A small proportion, approximately 10%, of those with a diagnosis of ASD also have a known genetic disorder such as Tuberous Sclerosis (TSC), fragile X syndrome, Prada-willi/Angelmann syndrome and Smith-Lemli-Opitz syndrome (Gillberg & Coleman, 2000; Muhle et al., 2004). This research proposes RSS is an additional disorder which is a risk factor for increased ASD.

Wiznitzer (2004) proposed three hypotheses for the increased incidence of ASD in those with TSC. First Wiznitzer (2004) proposed that the abnormal gene in those with TSC could be directly impacting on brain development, particularly in the areas thought to be dysfunctional in ASD. Alternatively, a direct interaction between the TSC gene and an ASD susceptibility gene could be causing the increased ASD incidence. The third hypothesis, and thought to be the most likely in the case of TSC, is a non-specific brain dysfunction as a consequence of the TSC complex, specifically the seizures seen in children with TSC or tuber location. Similarly it has been proposed that the association between ASD and Fragile X Syndrome (FXS) could be brain dysfunction as a result of low levels of FMRP, a protein critical for normal brain development (Hatton et al., 2006). However,

in the case of FXS it has also been suggested that the ASD is not true autism but brain pathology with similarities to that seen in ASD with overlapping behavioural profiles (Cornish et al., 2007).

An increased incidence of ASD in RSS could also be due to any of the three hypotheses Wznitzer (2004) proposed for TSC. While RSS is not associated with seizures or tuber development, as is seen in TSC, or a specific protein deficit, as seen in FXS, it is associated with an increased level of pre and peri-natal complications as a result of the syndrome. Some pre and peri-natal factors have been found to be risk factors for ASD.

Being born small for gestational age has been associated with a two fold increase in the incidence of ASD (Larsson et al., 2005; Hultman et al., 2002) and other risk factors include increased maternal age (Croen et al., 2007; Glasson et al., 2004; Hultman et al., 2002; Kolevzon et al., 2007; Larsson et al., 2005), prematurity (Williams et al., 2007; Cryan et al., 1996), low apgar score at 5 minutes (Hultman et al., 2002; Kolevzon et al., 2007) and caesarean section delivery (Maimburg et al., 2006; Glasson et al., 2004). All of these factors are associated with an increased incidence of complications, such as reduced nutrient supply, reduced oxygen supply and environmental insults during pregnancy, labour and delivery and it has been proposed that these complications during critical periods are sufficient to cause brain damage which can result in ASD like behaviours. Alternatively, it has been suggested that the additional brain insult, in those with a proportion of the ASD genes, causes the symptomology to become clinically significant, where it may have been the broader phenotype (Hultman et al., 2004; Volkmar, 2007). This pattern of interaction would be likely to result in the lesser variants of autism e.g. Asperger's syndrome, and would be consistent with a high risk of the broader phenotype in relatives (Volkmar, 2007).

The first aim of this research is to report the incidence of ASD in a RSS population. Further to this, those who meet criteria for ASD will be compared to the remainder of the RSS group to see if they form a homogenous group for pre and peri-natal characteristics, RSS symptomology or for one of the genetic mutations seen in RSS.

Study aims

- Compare the incidence of social and communication difficulties in children with RSS and an age and gender matched control group.
- Investigate the incidence of ASD in children with RSS
- Investigate whether children with RSS that meet criteria for ASD form a homogenous group relative to other children with RSS.

Method

Participants

Russell Silver Syndrome (RSS)

Parents and children aged 5-16 years with a diagnosis of Russell Silver Syndrome were recruited through the CGF. A total of 24 children with RSS were recruited to participate in this research.

Control Group

Control group participants were recruited by contacting parents and children at primary and secondary schools in Birmingham and Worcestershire and through e-mail shots in the School of Psychology at the University of Birmingham and through contacts of the researcher.

Full details of participant recruitment can be found in section 2.3, chapter 2 general methodology, of this thesis.

Table 4.6: Demographics of Russell Silver Syndrome group and Control group

	N	Birth weight (g) <i>M (SD)</i>	Gestational Age (weeks) <i>M (SD)</i>	Test Age (months) <i>M (SD)</i>
Russell Silver Syndrome (RSS)	24 (12 male, 12 female)	1920.50 (595.33)	37.04 (3.46)	117.00 (38.72)
Control	24 (12 male, 12 female)	3496.00 (446.01)	39.54 (1.06)	116.63 (36.62)

Measures and procedure

Parents of all children that participated in this research completed the Social Communication Questionnaire (SCQ; Rutter, Bailey & Lord, 2003) and returned this to the researcher. At this point

any child scoring greater than 15 on the SCQ was contacted. A home visit was arranged with these children, during which they completed the Autism Diagnostic Observation Scale- Generic (ADOS-G; Lord et al., 1998) with a trained professional. All children were also visited at home, on a separate occasion, during which they completed the BAS-II (Elliott et al., 1996). All children <8 years completed the early years battery, while those > 8 years completed the school age battery. Full findings from the BAS-II can be seen in Study 3 of this thesis. Full details of the measures used in this study can be found in Chapter 2, general methodology, of this thesis.

Results

Comparison of the RSS and control group on the SCQ and sub-scales.

Kolmogorov Smirnov Z tests showed that total SCQ scores for each group were normally distributed, however the distribution of contributing factors, social ability, communication and repetitive behaviours were not normally distributed therefore, total SCQ scores were compared using parametric analysis, but sub-scale scores were compared using the non-parametric comparison, Mann-Whitney U with an alpha of 0.05.

RSS children were found to score significantly higher on the SCQ than did control children ($t=3.53$, $p=0.002$). It can be taken from this that children with RSS are encountering more social and communication difficulties. Follow up analysis using the non-parametric Mann-Whitney U, revealed that while overall, the RSS group were displaying significantly more communication difficulties ($z=3.84$, $p<0.000$) and repetitive behaviours ($z=3.15$, $p=0.002$), they were not found to display significantly more social difficulties ($z=1.66$, $p=0.09$).

Follow up analysis

The SCQ guidelines (Rutter et al., 2003) recommend the use of a cut-off total score of 15 on the SCQ for further investigation. Total SCQ scores were assessed and revealed that six RSS participants met criteria for further investigation, while none of the control group scored >15 on the SCQ (see table 4.7).

It was proposed that all those who scored >15 on the SCQ would be followed up using the ADOS-G. However, of the six RSS participants who scored >15 on the SCQ, two had already

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received a diagnosis of Asperger's Syndrome and so did not require follow up. In addition it was impossible to visit one child (18) as they had moved away from the area after completion of the SCQ, so they were therefore excluded from any further analysis. The remaining three participants who scored >15 on the SCQ completed the ADOS-G.

Table 4.7 : Participant scores on the SCQ

Participant No.	Gender	RSS group	Age matched control group
1	M	19*	4
2	F	2	0
3	F	0	2
4	F	2	0
5	M	4	0
6	F	5	4
7	F	17*	2
8	M	16*	0
9	F	11	0
10	M	32**	0
11	M	10	4
12	F	5	2
13	M	3	5
14	F	4	10
15	F	1	0
16	M	28**	2
17	M	4	4
18	M	28*	2
19	M	8	4
20	F	6	4
21	M	3	4
22	M	7	0
23	F	2	1
24	F	7	4

*=Score above 15 without an ASD diagnosis

**=Score above 15 with an ASD diagnosis

Two of the three children who completed the ADOS-G were found to meet ASD criteria on both the SCQ and ADOS-G (see table 4.8) which shows that the female that was followed up only scored 2, while the two males both scored above the cut-off of 4 for Asperger's syndrome, with the 7 year old male also scoring >6, and therefore meeting criteria for Autism.

Table 4.8: ADOS-G breakdown of output for the three children which were further investigated.

	Male, 7 years	Female, 10 years	Male, 12 years
Communication			
Stereotyped/idiiosyncratic use of words or phrases	0	0	1
Reporting of events	2	0	0
Conversation	0	0	0
Descriptive, conventional, instrumental or informational gestures	1	0	1
Total (>3 - AD, >2 - AS)	3**	0	2*
Reciprocal social interaction			
Unusual eye contact	0	0	2
Facial expressions directed to others	0	1	1
Insight	2	0	1
Quality of Social Overtures	2	0	1
Quality of social response	1	0	1
Amount of reciprocal social communication	1	0	0
Overall quality of rapport	1	1	1
Social total (>6 - AD, >4 - AS)	7**	2	7**
Communication and social total (>10 - AD, >7 - AS)	10**	2	9*

*> cut off for ASD, **>cut off for AD

Of the 24 RSS children who participated in this research, four were found to meet ASD criteria, two on both SCQ and ADOS-G and two had received a formal ASD diagnosis. The estimated prevalence of ASD in RSS, based on these research findings, is 1.6 in every 10 RSS children.

Comparison of the Non-ASD RSS group with ASD RSS group

For the following analysis, the two participants who had received formal diagnosis of Asperger's syndrome were grouped with those who met ASD criteria on both the SCQ and ADOS-G to create a small ASD RSS group (N=4). The child who met only ASD criteria on the SCQ was grouped with the rest of the remaining RSS group to create a non-ASD RSS (N=19).

Between group comparisons, ASD-RSS and non-ASD RSS, were conducted using Mann-Whitney U, due to the uneven group sizes, and chi square analysis where appropriate. A conservative alpha of 0.001 was employed to reduce the risk of type 1 errors due to multiple comparisons.

The two groups, Non-ASD RSS and ASD RSS, were compared to the remainder of the group to see if they formed a homogenous group for birth weight, gestational age and maternal age, as these were all factors previously found to be important in the development of ASD. It can be seen, from table 4.9, that the two groups did not differ significantly for any of these factors.

The two groups, non-ASD RSS and ASD RSS, were also compared to see if they differed for incidence of diagnosis of MatUPD7, again the two groups were not found to differ (see table 4.9).

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Lastly, the non-ASD RSS and ASD RSS, groups were compared to see if they differed for the incidence of RSS symptom presentation, specifically asymmetry and facial features, once again the ASD RSS group were found to be comparable to the non-ASD RSS group (see table 4.9).

Table 4.9: Mann Whitney U and Chi Square comparisons of characteristics of ASD-RSS (n=4) and non-ASD RSS (N=19) groups.

	Non-ASD RSS <i>M (SD)</i> N=19	ASD RSS <i>M (SD)</i> N=4	Z/chi	p
Birth weight (g)	1811.95 (624.91)	2316.25 (118.42)	2.07	0.04
Gestational age (weeks)	36.74 (3.66)	37.75 (2.63)	0.34	0.74
Maternal Age (months)	396.75 (58.49)	340.75 (25.18)	1.80	0.08
Positive for MatUPD7	7	1	-	-
Negative for MatUPD7	8	0	-	-
Never been assessed for MatUPD7	4	3	-	-
Asymmetry (%)	12 (63%)	2 (50%)	0.49	0.49
Facial features (%)	16 (84%)	3 (75%)	1.02	0.31

Impact of ASD on cognitive ability

The cognitive ability, taken from the full assessment using the BAS-II, reported in Study 2 of this thesis, of the non-ASD RSS and ASD RSS groups were compared using a Mann-Whitney U analysis, this revealed that the overall cognitive ability of the two groups did not differ significantly ($z=1.02$, $p=0.310$).

Discussion

Initial comparisons were conducted comparing the mean scores of the RSS and control groups on the Social Communication Questionnaire (SCQ; Rutter et al., 2003). These revealed that overall the RSS group were displaying more social communication difficulties than the control group, however, these comparisons were only significant for communication and repetitive behaviours and not social behaviours. Analysis of individual scores revealed that the differences found between the two groups were most likely due to a small number of participants scoring particularly highly on the SCQ, rather than a general group effect. Further analysis was conducted, separating those who scored

> 15 on the SCQ and further investigating these for the presence of ASD using the ADOS-G (Lord et al., 1998).

The research revealed an incidence rate of ASD of 1.6 in every 10 children, or 160 in every 1000, with a diagnosis of RSS. This is far higher than the recent reported prevalence rate in the general population in the US of 6.7 in 1000 (Centre for Disease Control and Prevention in the US, 2007), almost a 25 fold increase.

One participant who met initial screening criteria for ASD, using the SCQ, in this research was not followed up and was excluded from the final analysis, had they been assessed the incidence rate may have been even higher than can be reported. It is possible that there was a recruitment bias in the RSS group, with those with the most behavioural problems consenting to participate. However, RSS as a syndrome is rare, with reported incidence of between 1 in 50,000 and 1 in 100,000 (Anderson, Viskochil, O’Gorman & Gonzales, 2002; Perkins & Hoang-Xuan, 2002). Using a mid-point calculation of 1 in 75,000 it can be estimated that there are at any one time approximately 120 children aged between 5 and 16 in the UK with RSS. If all these were tested and still only the four detected in this research met criteria for an ASD the incidence of ASD in RSS would still be 3.3 in 100 or 33 in 1000, a 5 fold increase on the incidence reported in the general population. It can therefore be summarised that RSS is a risk factor for ASD.

The ASD reported in the RSS population here, is all at the high functioning end of the autistic spectrum. The cognitive ability of children with RSS has been assessed, using the British Ability Scale-II (Elliott, Smith & McCulloch, 1996), as part of the larger project (see study 2). Here the general cognitive ability of children with RSS meeting ASD criteria was compared with the cognitive ability of those not meeting ASD criteria. Cognitive ability was not found to differ significantly between those with ASD and those without, with both groups having a mean cognitive score >100. Further support for the mild presentation of ASD in RSS can be seen in the fact that the two participants that met ASD criteria on two separate assessments had not been sufficient cause for concern at home or in school to be assessed for ASD, other than as part of this research.

Once the anecdotally reported increased incidence of ASD in children with RSS was established, this research compared those RSS-ASD and those RSS-Non-ASD, to see if the ASD

group formed a homogenous group either with reference to pre or peri-natal insults, RSS symptom presentation or genetically.

ASDs have been associated with specific pre and peri-natal insults including being born Small for Gestational Age (SGA; Larsson et al., 2005; Hultman et al., 2005), being born prematurely (Williams et al., 2007; Cryan et al., 1996), and having an increased maternal age (Williams et al., 2007; Glasson et al., 2004; Hultman et al., 2002; Kolevzon et al., 2007; Larsson et al., 2005).

One of the clinical symptoms of RSS is being born SGA. Being born SGA has previously been associated with a two fold increase in the incidence of ASD (Larsson et al., 20002; Hultman et al., 2005). It was hypothesised therefore that it is the degree to which birth weight is compromised that is key to the presence of ASD, with those born smallest for gestational age being at the biggest risk. All those in the RSS group here were born SGA, with the birth weight of ASD-RSS not differing significantly from that of the non-ASD RSS group, this suggests that degree of reduced birth weight, and the potential consequences of this, cannot account for the cases of ASD found here.

Although the majority of those with a diagnosis of RSS are born at term, a small percentage are born prematurely, due to concern for their intra-uterine growth. Prematurity has been associated with an increased prevalence of ASD (Williams et al., 2007; Cryan et al., 1996), so it was hypothesised that the RSS-ASD group would be those that had been the lowest gestational age, however the gestational age of those with RSS-ASD was not found to differ significantly from that of those in the RSS non-ASD group.

A final factor assessed which has been consistently found to be associated with an increased risk of ASD is increased maternal age (Williams et al., 2007; Glasson et al., 2004; Hultman et al., 2002; Kolevzon et al., 2007; Larsson et al., 2005). It could be hypothesised that the added complications associated with increased maternal age, could be acting in combination with the complications implicit in being born with RSS; here, however, the maternal age of those with ASD-RSS was not found to be significantly different from the rest of the RSS group.

Pre and peri-natal factors which have been associated with ASD in the past have not been found to be sufficient alone to differentiate the RSS-ASD group from the remainder of the group,

however, the RSS-ASD is small relative to the main RSS group and had this group been larger significant differences may have been detected on these factors.

The RSS-ASD group were not found here to create a homogenous group in RSS symptom presentation, two of the four showed body asymmetry, and three of the four were described as having different facial characteristics, this was representative of the variation in symptom presentation seen across the RSS group as a whole

Transmission of ASD is not a simple genetic inheritance pattern and there are multiple genes, possibly up to 15, involved (Risch et al., 2005). Reports of the broader ASD phenotype in relatives of those with ASD (Rutter, 2005; Volkmar, 2007) suggests that having only a proportion of the genes found in those with ASD results in a milder phenotype. Witzner (2004) proposed that in other genetic syndromes, such as TSC, the genetic mutation associated with the disorder could be acting directly with genes associated with ASD. Alternatively an environmental insult may be sufficient to cause brain damage in an individual, causing them to display ASD behaviours, when without the insult they may only have displayed the milder phenotype. This mechanism of transmission would be associated with the lesser variants of autism e.g. Asperger's syndrome, and would be consistent with a high risk of the broader phenotype in relatives (Volkmar, 2007).

MatUPD7 has been found in approximately 10% of children with RSS (Hannula, Kere, Pirnen, Holmberg & Lipsanen-Nyman, 2001; Hitchins *et al.*, 2001; Kotzot *et al.*, 1995), a further 35-40% may have a diagnosis of epigenetic mutation of chromosome 11p15 (Eggerman *et al.*, 2006; Schnoerr *et al.*, 2006). Unfortunately, as the second finding is fairly recent, the majority of children with RSS have not been assessed for it and, although a MatUPD7 is a well established genetic cause of RSS, there is still a large proportion of children who although having a diagnosis of RSS have not been assessed for MatUPD7, this was one of the main limitations of this research.

In the subgroup of children with RSS-ASD involved in the research here, only one had been assessed for MatUPD7 and they were found to be positive for the mutation. Therefore a genetic interaction with the matUPD7 cannot be excluded as the cause for the increased rate of ASD in the RSS group. However, being MatUPD7 RSS alone is insufficient as the cause for ASD as several of the other members of the non-ASD-RSS group also had this genetic mutation. It is important, in the

future, for the karotype of all those in the RSS-ASD group to be investigated with the hypothesis that they will all have MatUPD7. If this is not found to be the case the pre and peri-natal experience which form part of RSS could be hypothesised to be the risk factor for ASD in children with RSS. To further support this as the cause of the ASD in RSS, screening of immediate, and possibly the extended family, of children with RSS should reveal a higher incidence of broader ASD phenotype behaviours in the relatives of those with RSS-ASD.

Summary

In summary, RSS was found to be a risk factor for ASD. The mechanism by which this occurs, does not appear to be non-specific brain damage as a consequence of associated risk factors of the RSS as proposed at the most likely mechanism in TSC. It is hypothesised that children with RSS-ASD already have a susceptibility to ASD and either a pre natal environmental factor as a consequence of the RSS or a genetic mutation, potentially matUPD7, seen in children with RSS is interacting with the ASD susceptibility genes. RSS has been found to be associated with high functioning ASD, which is thought to most likely occur in children where there is a genetic susceptibility to ASD (Volker, 2007).

4.4 CHAPTER 4: DISCUSSION

The aim of this chapter was to investigate the behavioural profile of children with RSS. Study 3 used a screening questionnaire to investigate the incidence of conduct problems, emotional problems, hyperactivity, peer problems and overall behavioural problems in children with RSS. This study confirmed that parents report that children with RSS have significantly more behavioural problems than an age matched control group. This study then further investigated the incidence of symptoms of ADHD, hyperactivity/impulsivity and inattention, in children with RSS, and revealed that significantly more symptoms of ADHD were reported by parents of RSS children than control parents. Only significantly more symptoms of inattention were reported in RSS females, while RSS males reported significantly more hyperactivity/impulsivity and inattention, fitting with previous research findings that males display more externalising symptoms of ADHD than do females (Biederman, 2002; Levy et al., 2005). Study 2 of this chapter investigated the incidence of ASD in RSS, and revealed a significantly raised incidence relative to the national average, with all cases of children with RSS with ASD displaying high functioning ASD.

Previous research has suggested that being born Small for Gestational Age (SGA), as children with RSS are, significantly increases the likelihood of having both ADHD (Robson & cline, 1998) and ASD (Larsson et al., 2005; Hultman et al., 2002). It was therefore hypothesised in this research that birth weight would be key to the incidence of ADHD and ASD in RSS, this was however not found to be the case. The gestational age of the RSS children that participated was not found to differ significantly from that of the control group, therefore only research with children born SGA at term was relevant as a comparison for children with RSS. A review of this literature, revealed that post natal complications appeared to be key to the development of ADHD in children born SGA (Robson & Cline, 1998). RSS children are at an increased risk of post natal complications due to their poor feeding and weight gain, and this may have been a key mediator in the development of ADHD symptoms, the direct implication of post natal complications to ASD development has not been investigated.

What could not be excluded in this research was the importance of the genetics of RSS. As only a proportion of children that participated had been screened for matUPD7 and, at the time of testing, 11p15 was only newly discovered these genetic mutations could not be controlled for. Whether or not a child has MatUPD7 or an epigenetic mutation of 11p15, may be a key factor in the degree to which they display symptoms of ADHD and/or ASD. Only one of the four RSS children that had been found to be positive for ASD had been genetically screened and found positive for MatUPD7, therefore it remains critical that the other children with RSS ASD are genetically screened. As children with RSS, who had not been found positive for ASD, had also reported MatUPD7, this cannot be the full explanation for the raised incidence of ASD in RSS, however it can not be excluded that this genetic mutation is acting in a synergistic way with other genetic mutations known to be critical in the development of ASD.

This chapter has confirmed that children with RSS are at an increased risk of ADHD and ASD, and this has important implications for the RSS child both at home and in school. Further investigations are needed into why there is a raised incidence of both these behavioural disorders and this would have both implications for better and earlier detection, or possibly even prevention of the ADHD and ASD in children born with RSS in the future.

CHAPTER 5

THE PSYCHOSOCIAL PROFILE OF CHILDREN WITH RUSSELL SILVER SYNDROME

5.1 Overview of chapter

The aim of this chapter was to create an overview of the psychosocial profile of children with RSS. It was hypothesised that they may experience low self esteem and body image attitude as a result of being treated differently due to their short stature and phenotypical facial appearance.

Study 5– This study first directly assessed the self esteem of children with RSS, using age appropriate measures. It further went on to compare RSS and control group children for perceived and actual height, weight and face shape. It was hypothesised that whether or not a child with RSS had received GHT and parental heights would impact on their height attitude, therefore these factors were assessed in the RSS group.

Study 6 – This study differed from the rest that make up this thesis as it was not conducted with children with RSS. It aimed to see how others view children with RSS typical features, short stature and face shape, and how this impacted on trait attribution. It was hypothesised that peers and adults would attribute more baby like traits to a child with RSS features.

5.2 STUDY 5

SELF ESTEEM AND BODY IMAGE ATTITUDE IN RUSSELL SILVER SYNDROME

Abstract

Objectives: The aim of this study was to compare the self esteem of RSS children with that of age matched controls and to assess the body image attitude of the two groups to see whether RSS children had a more negative body image, as this could be a mediatory factor for reduced self esteem. In addition factors which could impact on height attitude, such as GHT and parental height, were assessed for impact in the RSS group. **Method:** Twenty children with RSS and twenty age matched control children participated. All participants completed an, age appropriate, measure of self esteem and a body image attitude scale which assessed perception and satisfaction with height, weight and face shape. Parents provided actual body measurements. **Results:** The self esteem of the RSS children was not found to differ from that of the control children. Children with RSS were found to be significantly shorter and lighter than control group children, and perceived themselves as being shorter and less satisfied with their height than did control children. Both males and females with RSS were found to be dissatisfied with their height. No group differences in weight perception or satisfaction were found, apart from control females reporting that they would like to be slimmer, while RSS females wanted to be heavier. RSS children were not found to perceive themselves as facially different, and were not dissatisfied with their facial shape. **Discussion:** Although children with RSS were shorter and lighter than control children and perceived themselves to be shorter, this was not found to have had a negative impact on their self esteem. RSS males were not found to perceive themselves as short, though RSS females were, possibly reflecting the fact that short stature is more of a stigma in males. RSS children over 8 years were found to perceive themselves as shorter and less satisfied with their height than control children, while RSS children under 8 years were not found to differ, possibly reflecting the increasing importance of height with age.

Perceived and actual body shape and the correlation with self esteem in children with Russell Silver Syndrome (RSS)

RSS is characterised by low birth weight, short stature, and a phenotypical facial appearance (Wollmann et al., 1995; Price et al., 1999), along with feeding difficulties from birth (Price et al., 1999), meaning that, in most cases, RSS children are very slim. It is thought that the physical features of RSS may put them at risk of having a negative body image attitude and, in turn, this could be having a detrimental effect on their self esteem.

Short Stature

There is a stereotypical belief that short children are at a disadvantage (Gilmour & Skuse, 1996; Clopper, 1994; Harper, 2000; Loh, 1993; Law, 1997; Law, 1987; Eisenberg et al., 1984; Holmes et al., 1982; Wake, Coghlan & Hesketh, 2000) with even doctors reporting that short stature children would benefit from receiving Growth Hormone Treatment (GHT) to increase their height (Cuttler et al., 1996).

With the advent of recombinant GHT, short stature became a treatable condition. Large numbers of children, particularly males, are now referred to growth clinics for assessment, and potentially treatment, for short stature. As there is now a treatment option for short stature, there has also been an increased research interest into the psychological consequences of having short stature.

Studies with short stature children recruited through growth clinics (referred sample), have generally reported more psychosocial problems, including low self esteem, low social competence and social difficulties, in short stature children than in control children (Visser-van Balen, Sinnema & Geenan, 2006 for review; Gordon et al., 1982; Sandberg et al., 1994; Stabler et al., 1998; Gilmour & Skuse, 1996). However, referred samples are biased towards the recruitment of those with the most awareness of their short stature (Bussbach et al., 1998). Referred short stature samples have been found to report more problem behaviours (Kranzler et al., 2000) and poorer coping skills in adulthood (Bussbach et al., 1998), than those with short stature that had not been referred.

Studies with clinic-referred short stature populations tend to exclude participants with a known organic cause for their short stature, such as RSS. Groups that are referred to clinics with a syndrome, of which one symptom is short stature, may not be best represented by the research

findings from studies with referred idiopathic short stature children (short stature with no known organic cause). For groups with an organic cause for their short stature the primary reason for attending clinics may not be stature, and they may not perceive themselves as 'short stature', but as having a syndrome, short stature is just part of that syndrome. In addition, a significant proportion of children with RSS, and other syndromes with short stature, are more likely to be receiving GHT and this in itself has been found to have a positive impact on self esteem and body image attitude (Boulton et al., 1991).

Perception of stature in children appears to be important. It has been found that when children and their parents perceive themselves/their child to be taller than they are, there was an increase in the self esteem of the child (Hunt, Hazen & Sandberg., 2000), with perceived, rather than actual height, having the biggest impact on reported psychosocial difficulties. It is important therefore to investigate how children with RSS perceive themselves, and their body image attitude, as this may have a bigger impact on self esteem than actual height.

Low weight

The majority of body satisfaction research, assessing the affect of body weight, has focused on the effects of being overweight, with limited research in to the psychological effects of being underweight, as is commonly seen in RSS. In Western cultures, such as the UK, there is a thin ideal, with overweight people being perceived by adults and children as less attractive, intelligent, competent and disciplined, and more lazy (Tiggerman and Rothblum, 1997; Hill, 1995; Tiggerman, 1998).

It is common for children and adolescents to show a desire to change their weight, with an increased desire being associated with emotional distress (Johnson & Wardle, 2005), reduced global self worth, and general dissatisfaction with other areas of their lives (Mendelson et al., 1996). Body image, for weight, has been shown generally to have a positive correlation with self esteem and depression (Mintz & Betz, 1986), with both body image dissatisfaction, and therefore low self esteem and depression, increasing with age (Beerman et al., 2006; Gardner et al., 1997; Maloney et al., 1996).

It has generally been found that there is a greater drive to be thin in girls than boys (Stice & Beerman, 2001). Ricciardelli & McCabe (2001; review) reported that only between 4-18% of girls

would like to be bigger, while 25-58% reported that they would like to be thinner, being smaller was perceived on the whole as positive. In males there has often been a split described, with some boys wishing to increase their body weight, usually through increased muscle bulk, while others mimic the findings in girls with a drive for thinness (Smolak, 2000; McCabe & Ricciardelli, 2001; 2004; McCabe et al., 2001; Cohane & Pope, 2000).

While there is little research to suggest that RSS females will be unhappy being slim, as this has generally been found to be the ideal body weight in our culture, it still remains a possibility and what appears to be more important is the level of satisfaction they have with their weight. If the RSS child found their low weight dissatisfying, then it could be impacting on their self esteem. The prediction for RSS males however, could be more complicated, the ideal for males puts more of an emphasis on muscle bulk, so a greater weight may be more desirable. Again though, how satisfied the males feel with their weight is key to the impact it could have on self esteem.

Face Shape

The final feature of RSS, which will be assessed in this study, is their face shape. The features of an RSS child's face, in many ways mimic the features of a baby's face, large eyes, eyes in the centre of the vertical plane of the face, narrow face and a large protruding cranium (Berry & McArthur, 1985; Zebrowitz-McArthur & Berry, 1987; Zebrowitz & Montepare, 1992; Masip, Garrido & Herrero, 2004)

Due to the similarities in facial appearance of babies and RSS children, it can be anticipated that children with RSS will be seen as more naïve, weaker and warm hearted than other children by adults and children, as has been demonstrated in previous research with baby faced individuals (Zebrowitz & Montepare, 1992; Zebrowitz, Olson & Hoffman, 1993; Berry & McArthur, 1985; Berry & Brownlow, 1989; Masip *et al.*, 2004). The impact on self esteem of being treated as younger than actual chronological age, due to having baby-like facial features, is unknown.

It has been found, generally, that those who feel unconditionally accepted for their physical appearance are least likely to show body dissatisfaction and are least likely to have a reduced self esteem (Beerman et al., 2006). This may be an important consideration with children with RSS, who

on the whole, have been observed to be encouraged by their parents to have confidence in their appearance, height, weight and facial features.

This research study is two fold, first the self esteem of children with RSS will be assessed in comparison to an age matched control group; it is anticipated that the self esteem of children with RSS will lower than that of the age matched control group. Following from this, analyses will be made of how the participating children see their, height, weight, and face shape, to assess for dissatisfaction. It is predicted that RSS children will perceive themselves to be shorter, lighter and more baby-faced than control children, and will display significantly more dissatisfaction with their physical appearance.

Study aims:

- Comparison of the self esteem and body image attitude of children with RSS and a gender and age matched control group.
- Investigation of the effects of age and gender on self esteem and body image attitude.
- Assessment of the impact of parental heights and growth hormone treatment on height perception and satisfaction, and self esteem.

Method

Participants

Russell Silver Syndrome (RSS)

Parents and children aged 5-16 years with a diagnosis of Russell Silver Syndrome were recruited through the CGF. A total of 24 children with RSS were recruited to participate in this research. Of these 24, a 4 did not participate due to their refusal to complete one of the two scales used here, or because their age matched control refused to complete one of the scales. Demographic details of the group can be seen in table 1.

Control Group

Control group participants were recruited by contacting parents and children at primary and secondary schools in Birmingham and Worcestershire and through e-mail shots in the School of Psychology at the University of Birmingham and through contacts of the researcher.

Full details of participant recruitment can be found in section 2.3, chapter 2 general methodology, of this thesis.

Table 5.1: Demographics of RSS and control groups

	N	Birth weight (g) <i>M (SD)</i>	Age at testing (months) <i>M (SD)</i>	Height now (cm) <i>M (SD)</i>	Height now (centile) <i>M (SD)</i>
Russell Silver Syndrome	20 (10 male, 10 female)	1877.85 (596.73)	118.85 (40.44)	124.20 (20.17)	9.00 (15.92)
Control	20 (10 male, 10 female)	3454.14 (461.71)	118.95 (38.06)	137.11 (20.61)	55.94 (31.28)

Measures and procedure

This research used two measures of self esteem, the Pictorial Scale of Perceived Competence and Social Acceptance for Young Children (PSPCSA; Harter & Pike, 1984) with children under 8 years, and the Self Perception Profile for Children (SPPC; Harter, 1985) with participants over 8 years. Children that completed the PSPCSA, did so with the researcher during a home visit, where they also completed the BAS-II (Elliott et al., 1996; see study 2 of this thesis). Children that completed the SPPC, also did this during the home visit, though independently of the researcher. All children also completed the body image attitude scale, based on the scale used by Dowdney et al., (1995), during their home visit. Full details of the measures used in this study can be found in chapter 2 of this thesis, general methodology.

Results

Kolmogorov Z tests indicated that data was normally distributed and box plot analysis revealed that there were no outliers, therefore parametric analysis was used throughout.

Self Esteem

RSS and control group children were compared, using an independent samples t-tests, for the components measured in the PSPCSA (Harter & Pike, 1984) and SPPC (Harter, 1985). Findings can be seen in table 5.2.

Table 5.2: Independent sample t-test comparison of RSS and control group for self esteem factors of the PSPCSA (N=22) and SPPC (N=18).

	PSPCSA (<8 years of age)				SPPC (> 8 years of age)			
	RSS (N=11) <i>M (SD)</i>	Control (N=11) <i>M (SD)</i>	t	p	RSS (N=9) <i>M (SD)</i>	Control (N=9) <i>M (SD)</i>	t	p
Cognitive	3.14 (0.70)	3.23 (0.68)	0.30	0.76	-	-	-	-
Physical	3.15 (0.70)	2.72 (0.47)	1.66	0.11	-	-	-	-
Social	3.04 (0.79)	3.19 (0.57)	0.09	0.63	-	-	-	-
Maternal	3.05 (0.71)	2.68 (0.50)	1.41	0.17	-	-	-	-
Scholastic	-	-	-	-	2.39 (0.61)	2.83 (0.72)	1.43	0.17
Social	-	-	-	-	2.81 (0.62)	2.96 (0.64)	0.51	0.62
Athletic	-	-	-	-	2.32 (0.62)	2.85 (0.54)	1.95	0.07
Physical	-	-	-	-	2.33 (0.97)	2.31 (0.69)	0.05	0.96
Behavioural	-	-	-	-	2.63 (0.99)	3.20 (0.70)	1.42	0.18
Global Self Worth	-	-	-	-	2.63 (0.80)	3.26 (0.58)	1.90	0.08

As can be seen in table 5.2, RSS and control group children were not found to differ on any factor of self esteem assessed, in either the younger (< 8 years of age) or older (> 8 years of age) groups.

Body Image

The mean height centile, mean weight centile (calculated using Child Growth Foundation Software, 1996) and BMI of the RSS and control children were compared. RSS and control children were then compared for their mean placement, ideal and satisfaction on the weight, height and face shape components of the BIAS (see table 5.3 for results).

Table 5.3: Independent sample t-test comparison of whole RSS group (N=20) and the whole control group (N=20)

	RSS (N=20) <i>M (SD)</i>	Control (N=20) <i>M (SD)</i>	t	p
Actual Height (Centile)	8.40 (15.00)	59.29 (30.12)	6.71	0.00*
Actual Weight (Centile)	8.39 (16.29)	57.73 (27.06)	6.99	0.00*
BMI	15.29 (2.24)	17.92 (4.16)	2.49	0.02*
Height I am	2.05 (1.15)	3.50 (1.15)	4.00	0.000*
Ideal Height	3.90 (1.13)	3.90 (0.92)	0.00	1.00
Height Dissatisfaction	1.85 (1.39)	0.40 (1.14)	3.61	0.001*
Weight I am	2.40 (1.20)	3.05 (0.89)	2.06	0.05
Ideal weight	2.60 (1.05)	2.55 (0.83)	0.17	0.87
Weight dissatisfaction	0.40 (0.94)	-0.40 (1.19)	2.36	0.02*
Face I have	2.65 (1.14)	2.90 (0.55)	0.89	0.38
Ideal face	2.55 (1.23)	3.10 (0.97)	1.57	0.13
Face dissatisfaction	0.00 (1.52)	0.20 (0.95)	0.50	0.62

It can be seen from table 5.3, that as a whole group the RSS children were significantly shorter and lighter than the control group, and they had a significantly lower BMI.

Overall the RSS placed themselves as shorter, on the BIAS, with a comparable ideal height to the control group, and in turn they were found to have significantly more height dissatisfaction than the control group. RSS children were not found to rate themselves as lighter than control group children, nor were their ideal weights significantly different, although there was a significant group difference for weight satisfaction, although this was due to the fact that the RSS group wanted to be heavier while the control group wanted to be lighter. RSS and control group children did not differ for perception of face shape, ideal face shape of face shape satisfaction.

Table 5.4 shows the same comparisons, as conducted for the whole group, between RSS and Control groups splitting the group by gender to make comparisons between RSS and control males only, and RSS and control females only.

RSS males and females were found to be significantly shorter and lighter than control males and females. While the perceived height of RSS females was significantly shorter than controls, the perceived height of the RSS and control males was comparable. However, the RSS males ideal height was significantly greater than controls while the RSS and control females were comparable. In turn both RSS males and females were significantly less satisfied with their height than controls. While Control and RSS males had no significant differences in perceived, ideal or weight satisfaction, control and RSS females were found to differ for weight satisfaction only. No significant group differences were found for face shape perception, ideal or satisfaction for males, but RSS females perceived their face shape as pointier and in turn their ideal was also significantly pointier (see table 5.4).

A comparison of RSS and control children <8 years of age and those >8 years, revealed again, in both groups, that RSS children were shorter and lighter than controls. Younger RSS and control children did not differ significantly for perceived height or ideal height, but were found to be significantly more dissatisfied with their height, while older children with RSS perceived themselves as shorter and more dissatisfied with their height. Neither younger or older children with RSS were found to rate themselves as lighter, as having a different ideal weight or more weight dissatisfaction. While the younger children were not found to perceive their face shape or ideal as control children, older children rated their face shape as pointier (see table 5.4).

Table 5.4: Comparison of RSS and control males (N=20) and of RSS and control females (N=20) for actual height, actual weight, BMI, and BIAS scales. Comparison of RSS and controls < 8 years (N=22) and of RSS and control > 8 years (N=18), for actual height, actual weight, BMI, and BIAS scales

	Male				Female			
	RSS <i>M (SD)</i>	Control <i>M (SD)</i>	t	p	RSS <i>M (SD)</i>	Control <i>M (SD)</i>	t	p
Actual Height (centile)	13.95 (19.32)	50.84 (36.17)	2.85	0.01*	2.85 (5.78)	67.74 (22.07)	9.00	0.000*
Actual Weight (Centile)	13.06 (22.01)	46.50 (24.51)	3.20	0.005*	3.72 (5.26)	68.95 (25.78)	7.84	0.000*
BMI	15.02 (2.30)	16.35 (1.62)	1.49	0.15	15.56 (2.26)	19.48 (5.33)	2.14	0.05
Height I am	2.7 (1.35)	3.1 (1.30)	0.73	0.46	1.4 (0.52)	3.9 (0.99)	7.05	0.00*
Ideal Height	4.7 (0.67)	3.9 (0.88)	2.29	0.03*	3.1 (1.38)	3.9 (0.99)	1.49	0.15
Height Satisfaction	2.00 (1.3)	0.8 (0.79)	2.45	0.03*	1.7 (1.49)	0.0 (1.33)	2.68	0.02
Weight I am	2.4 (1.17)	3.0 (0.95)	1.26	0.22	2.4 (1.08)	3.1 (0.88)	1.60	0.13
Ideal weight	2.9 (0.99)	2.7 (0.95)	0.46	0.65	2.3 (1.06)	2.4 (0.70)	0.25	0.81
Weight Satisfaction	0.5 (0.97)	-0.10 (1.52)	0.05	0.31	0.3 (0.95)	-0.7 (0.67)	2.72	0.01*
Face I have	3.0 (1.24)	2.7 (0.48)	0.71	0.49	2.3 (0.95)	3.1 (0.57)	2.29	0.03*
Ideal face	3.1 (1.37)	3.1 (0.99)	0.00	1.00	2.0 (0.82)	3.1 (0.99)	2.70	0.02*
Face Satisfaction	0.10 (1.66)	0.40 (1.07)	0.48	0.64	-0.1 (1.45)	0.00 (0.82)	0.19	0.85
	Younger (<8 years)				Older (>8 years)			
	RSS <i>M (SD)</i>	Control <i>M (SD)</i>	t	P	RSS <i>M (SD)</i>	Control <i>M (SD)</i>	t	P
Actual Height (centile)	6.36 (16.10)	52.10 (31.45)	4.29	0.001*	10.90 (14.05)	68.07 (28.34)	5.42	0.000*
Actual Weight (Centile)	8.23 (19.61)	47.06 (26.43)	3.91	0.001*	8.59 (12.23)	70.76 (22.76)	7.22	0.000*
BMI	14.23 (1.39)	15.56 (1.16)	2.50	0.021	16.59 (2.46)	20.76 (4.78)	2.33	0.034
Height I am	2.0 (1.26)	3.0 (1.26)	1.85	0.08	2.11 (1.05)	4.11 (0.60)	4.95	0.00*
Ideal Height	4.18 (1.25)	3.22 (1.08)	0.73	0.47	3.56 (1.42)	4.0 (0.71)	0.84	0.41
Height Dissatisfaction	2.18 (1.47)	0.82 (1.25)	2.34	0.03*	1.44 (1.24)	-0.11 (0.78)	3.19	0.006*
Weight I am	2.09 (0.94)	2.64 (0.81)	1.49	0.16	2.78 (1.20)	3.56 (0.73)	1.66	0.12
Ideal weight	2.36 (1.21)	2.27 (0.79)	0.21	0.84	2.89 (0.78)	2.89 (0.78)	0.00	1.00
Weight dissatisfaction	0.64 (0.92)	-0.36 (1.43)	1.95	0.07	0.11 (0.93)	-0.44 (0.88)	1.30	0.21
Face I have	3.0 (1.26)	2.63 (0.50)	0.87	0.39	2.22 (0.83)	3.22 (0.44)	3.18	0.006*
Ideal face	2.18 (1.40)	3.00 (1.26)	1.43	0.17	3.00 (0.87)	3.22 (0.44)	0.69	0.05
Face dissatisfaction	-0.64 (1.36)	0.36 (1.29)	1.77	0.09	0.78 (1.39)	0.00 (1.00)	1.67	0.11

What effect does receiving GHT have on height perception?

A comparison was conducted of the perceived height, ideal height and height satisfaction of those with RSS who had received GHT and those who had not received GHT. No significant differences were found between the groups for perceived height ($t=2.91$, $p=0.78$), ideal height ($t=0.50$, $p=0.62$) or height satisfaction ($t=0.73$, $p=0.48$).

What effect does receiving GHT have on self esteem?

Table 5.5: RSS group only: Comparison of self esteem factors of those that have and have not received GHT, using mann whitney U, participants < 8years

	GHT (N=8) <i>M (SD)</i>	No GHT (N=3) <i>M (SD)</i>	Z	p
Cognitive	3.15 (0.38)	3.11 (1.40)	0.83	0.50
Peer	3.36 (0.47)	2.61 (1.06)	1.13	0.28
Physical	3.06 (0.74)	3.00 (1.09)	0.00	1.00
Social	3.15 (0.61)	2.80 (1.06)	0.82	0.50

Table 5.6: RSS group only: Comparison of self esteem factors of those that have and have not received GHT, using mann whitney U, participants > 8years

	GHT (N=6) <i>M (SD)</i>	No GHT (N=3) <i>M (SD)</i>	Z	p
Scholastic	2.25 (0.54)	2.66 (0.76)	1.06	0.38
Social	2.64 (0.68)	3.17 (0.34)	1.30	0.26
Athletic	2.61 (0.52)	1.72 (0.25)	2.07	0.05*
Physical	2.50 (1.03)	2.00 (0.93)	0.78	0.55
Behavioural	2.44 (1.14)	3.00 (0.60)	0.65	0.55
Global Self Worth	2.52 (0.87)	2.84 (0.76)	0.26	0.91

*= $p < 0.05$

In the younger RSS group (<8years), there was no effect of whether or not they had received GHT on any level of their self esteem (see table 5.5), however data was only available for a small group so must be treated with caution. For the older RSS group (>8 years) whether or not they were receiving GHT had a significant effect on their perceived athletic competence (see table 5.6), with those that had received GHT perceiving themselves as more athletically able. There were no significant effects of receiving GHT on any other self esteem factor.

Does parental height effect height perception?

Maternal height was not found to correlate with height they perceived themselves to be ($r=0.06$, $p=0.9=82$), height they wanted to be ($r=0.14$, $p=0.57$) or height satisfaction ($r=0.14$, $p=0.056$). Paternal height too was not found to correlate with perceived height ($r=0.30$, $p=0.22$), ideal height ($r=0.18$, $p=0.58$) or height satisfaction ($r=0.12$, $p=0.62$).

Discussion

Self Esteem

Overall, RSS children were not found to have a lower self esteem than were control group children, this was found to be true of both the children that completed the PSPCSA (<8 years; Harter & Pike, 1984) and those that completed the SPPC (>8 years; Harter, 1985). This finding did not follow the hypothesis of this research, that children with RSS would have a lower self esteem as a consequence of different experiences due to their short stature, low weight and phenotypical facial appearance.

Further analyses conducted in this study looked at whether the RSS children were in fact seeing themselves as different to the control group for height, weight and face shape, because unless they were perceiving themselves as particularly short, thin or phenotypically face shaped, this was unlikely to impact on their self esteem.

Body Image Attitude – Whole Group

The RSS children that participated in this research were found to be shorter and lighter than control group children, as was expected (Price et al., 1999; Wollmann et al., 1998). As a whole group the RSS children were found to rate themselves as significantly shorter than did control children, and demonstrated dissatisfaction with their height. RSS children however, did not rate themselves as thinner than control children, though group differences for weight satisfaction were found, with RSS reporting they would like to be bigger and controls smaller. There were no significant group differences for face shape perceived, ideal or satisfaction.

It was expected that RSS children would be aware of their short stature, they regularly attend growth clinics, which would put emphasis on their stature. Previous research has demonstrated that being referred to clinics for short stature assessment can be detrimental. Short stature children, who were referred in childhood, were found to have significantly more long term self esteem and coping problems, than equally short statured peers that had not been referred (Bussbach et al., 1998; Kranzler et al., 2000), with perceived short stature more detrimental to self esteem than actual stature (Hunt et al., 2000). Guided by these research findings, it would have been expected that as the children with RSS were both a referred group, and reported that they were aware that they were short, their self

esteem would have been impacted, but this was not found to be the case. Research findings with referred groups, on the whole, work with children with idiopathic short stature. In RSS there is an organic cause and short stature is one of many symptoms that they have. Having a known cause for the short stature in RSS may be acting as a cognitive buffer for effects on their self esteem. In addition, approximately 70% of children with RSS will receive GHT to increase their adult height and this has previously been related to an increased self esteem (Boulton et al., 1991). However, further analyses conducted here found no difference in self esteem or height perception in those children with RSS that had received GHT.

Although the RSS children that participated in this study were found to be lighter than the control children, they did not report that they thought they were slimmer and weight dissatisfaction was due to control children wanting to be thinner. Self esteem has previously been found to positively correlate with body weight (Mintz & Betz, 1986) and therefore the RSS group were slim, and were not reporting that this was an issue, this would not have been expected to impact on self esteem.

Body Image Attitude – Gender Differences

Both RSS males and RSS females were found to be shorter and lighter than control males and females, as was expected (Price et al., 1999; Wollmann et al., 1995). RSS males, were not found to report that they thought they were shorter than did control males, but their ideal height was taller and in turn they were less satisfied with their height. RSS females, however, reported that they were shorter than control females, but with comparable ideal heights, so again they were found to have significantly more height dissatisfaction.

There is more stigma attached to short stature in males than females and this can clearly be seen in the bias towards males, with idiopathic short stature, being referred to growth clinics, with the average height of a referred male being greater than the average height of a referred female (Grimberg et al., 2005; Kranzler et al., 2000). What may have been happening in the case of the RSS males here is that they were not choosing honestly on the scale; they did not want to be the shortest because there is a certain degree of stigma attached to this. RSS females, however, may be more accurately reporting where they were on the height scale, as they were less influenced by the stigma of short stature. It

would have been interesting to compare the self esteem of the RSS male and RSS female, it would be expected, that if this proposal, that the RSS male is less accepting of their stature, were true, that this could have impacted on the self esteem of the RSS male but not the female. It was impossible in this study to look at self esteem split by gender, using two measures of self esteem, one with those < 8years and one with those >8 years. This would have meant splitting a relatively small RSS group, a further group division by gender would have made the groups very small and any significant finding weak.

RSS males and RSS females were both found to be significantly lighter for their age, than were control males and control females. Both RSS males and RSS females however did not perceive that they were thinner than their peers. The BMI of both RSS males and RSS females was found to be within a normal range and both genders were therefore less likely to see themselves as particularly thin as they were of an appropriate weight for their height.

The only significant gender finding for weight was that RSS females wanted to be bigger, while the control females wanted to be thinner, which was reflected in the significant difference in weight satisfaction between controls and RSS, an effect not reported in the males. In the UK there is a thin ideal and this has been found to be more salient with females than males (Stice & Beerman, 2001). Males have not generally been found to display the same drive for thinness as females, with some wishing to be bigger, through increased muscle bulk, while others would like to be thinner (Smolak, 2000; McCabe & Ricciardelli, 2001; 2004; McCabe et al., 2001; Cohane & Pope, 2000). The lack of findings for males here may represent a split in both the RSS and control groups, some wishing to be bigger, while others wish to be smaller, with the overall effect of balancing perceived weight and weight satisfaction in each of the groups.

RSS males, were found to report that they had a different face shape to those in the control group and did not differ significantly from the control group for ideal face shape or face shape satisfaction. RSS females rated themselves as having a more pointed chin and in turn their ideal face shape was more similar to their perceived face shape.

Body Image Attitude – Age Differences

RSS children < 8 years and RSS children > 8 years were again both found to be shorter and lighter than control groups. The younger RSS group was not found to differ significantly from the control group for perceived height, weight or face shape, ideal height, weight or face shape or weight or face shape satisfaction relative to the control group, however, they were significantly more dissatisfied with their height. The older RSS group however were found to rate themselves as shorter and more dissatisfied with their height, and reported wanting a pointier face shape.

The difference, between groups, in height perception is likely to be due to the importance of height with increasing age. At younger ages all children are relatively short, they will all encounter difficulties with their height, such as not being able to reach things, however, at older ages, being short becomes more salient as it becomes restricting. Interestingly weight also increases in importance with age, body dissatisfaction and an associated low self esteem have both been reported as greater in adolescents than children (Beerman et al., 2006; Gardner et al., 1997; Maloney et al., 1996), however, it was found that regardless of age RSS children were more dissatisfied with their height.

It has previously been demonstrated that receiving GHT (Boulton et al., 1991), can positively impact on self esteem and body image attitude. In this research it was shown that in younger children with RSS that whether or not they were receiving GHT had no significant effect on any level of their self esteem. This may have been the expected finding, as already stated, younger children are likely to be less aware of their stature or the implications of receiving GHT. In the older group there was one significant effect of receiving GHT and this was increased perceived athletic competence, possibly due to the biological effects of GHT rather than a psychological effect. If the effect was psychological there would have been expected increases in other areas of self esteem, which was not found.

The final point this study attempted to look at was the effect of parental height on perceived height, ideal height and height satisfaction. Previous research has shown that perceived height is more important than actual height (Hunt et al., 2000), it was therefore predicted that those children with the taller parents would perceive themselves as shorter, or have a taller ideal. Neither of these were found to be the case, with no correlation between parental heights and perceived or ideal height. This suggests that parental heights are not that important to how RSS children perceive themselves.

Summary

Overall the RSS children were found to be physically shorter and lighter than the control group, although they were found to have a comparable BMI, which indicates that their height and weight was in proportion. The RSS and control groups were not found to differ for reported self esteem and this was despite the RSS group perceiving themselves as shorter and more dissatisfied with their height than the control group. Previous research has suggested that perceived short stature has a detrimental effect on self esteem (Hunt et al., 2000) which was not found in this research. It is proposed that the short stature seen in RSS has a cause, and that many RSS children are receiving GHT, this may act as a cognitive defence buffer for the effect of perceived short stature on self esteem.

Some gender differences were reported here, with males not reporting that they were significantly smaller than control males, while RSS females did report being significantly shorter and more dissatisfied with their height. It is proposed that this effect was due to the stigma attached to short stature in males, encouraging the RSS males to choose height slightly higher on the height scale than they actually were; in turn their ideal height was found to be slightly higher.

Control females were found to be more dissatisfied with their height than RSS females, and wanted to be smaller, this suggests that the slim build in RSS is actually likely to be a positive feature, although that is only likely to be true in cultures, such as the UK where the ideal is thin.

Older RSS children were found to rate themselves as shorter and more dissatisfied with their height than controls, while younger RSS children were not found to differ significantly. This is likely to be due to the increasing importance of height with age, as short stature begins to be restricting.

RSS children did perceive differences in their physical appearance, but positively, and this did not impact on their self esteem. What is likely to be most important is that no matter how they perceive themselves, it is how they are accepted for their physical appearance (Beerman et al., 2006) that is important for their self esteem. The findings from this research suggest that RSS children are well accepted.

5.3 STUDY 6

RUSSELL SILVER SYNDROME: EFFECT OF FACE SHAPE AND HEIGHT ON TRAIT ATTRIBUTIONS

Abstract

Objective: The aim of this study was to assess the effect changes in facial features and stature of a child, had on trait attributions. Facial changes were made to mimic the facial features seen in RSS. It was hypothesised that the RSS typical facial features and short stature conditions would be rated, by adults and children, as having more infantile physical and personality traits. **Method:** Photographs of four male children and four female children were manipulated to create six conditions for each gender. The conditions were due to manipulations the facial features (RSS typical or control) and height (short, average, or tall) of one 'target' child. Undergraduates and children were asked to rate one version of the target male and one of the target female on 10 traits, four physical and six personality traits. **Results:** Adults were found to rate both males and females as more physically infantile, dependent on height, though there was not found to be an effect of height on personality trait attribution. No effect of face shape was found on physical trait attribution. Children were found to report the female picture as differing physically between face shape conditions, however, this was not found to impact on personality trait attribution. Height was not found to have a significant effect on physical or personality trait attribution for the female picture. No affect of height and face shape were reported for the male picture **Discussion:** Overall, the findings from this research were positive, even when physical differences were found, these were not found to impact on personality trait attributions, by either the adults or children.

Russell Silver Syndrome: Effect of face shape and height on trait attributions

It has been proposed that the short stature and phenotypical facial appearance of children with Russell Silver Syndrome (RSS) could impact on how they are perceived, and treated, by their peers and adults. Being treated differently could in turn be impacting on the self esteem and body image attitude of children with RSS. This study, working with children and adults, attempts to see how the two main features of RSS, short stature and phenotypical facial appearance impacts on the extent to which they are attributed infantile traits.

It is known that physical affordances guide what we think about others and in turn guides our expectations of them (Santos & Young, 2005), due to the assumption that perceptible attributes will provide information about behavioural traits (Masip et al., 2004; McArthur & Baron, 1983). Over generalization of rules based on physical appearance can lead to the prediction of incorrect behavioural traits (Zebrowitz et al, 2003).

RSS children are described as having “apparent facial triangularity” (Wollmann et al., 1997), with a relatively large head circumference in comparison to other facial measurements, with the impression of a small jaw and low placement of facial features. Facially, the features of RSS mimic those seen in infants. Large round eyes, a narrow chin, a large forehead, lower placed facial features and a head too large for their body, all features seen in RSS, are also recognisable features of an infant (Berry & McArthur, 1985; Zebrowitz-McArthur & Berry, 1987; Lorenz, 1943; McArthur & Apatow, 1983). In infants these features are such that facial affordances elicit a nurturing response from caregivers (Lorenz, 1943; Masip *et al*, 2004; Alley, 1988) thereby increasing the infant’s chance of survival.

Adults who have facial similarities to infants have been found to be rated as warmer, more honest, physically weaker, more submissive, more naive and kinder than adults with few infantile facial similarities (Berry & McArthur, 1985; Masip *et al*, 2004; McArthur & Apatow, 1983), this is indicative of an overgeneralization of infantile traits, based on physical appearance and was not found to be directly linked to estimated age (McArthur & Apatow, 1983).

Children with infantile facial features, in photographs, have been rated by adults as less cognitively capable with regards to household chores (Zebrowitz, Kendall, Tackett & Fafel, 1991) and

less likely to misbehave intentionally (Langlois *et al*, 1996). In real life situations, children with infant facial features were found to elicit a greater degree of maternal supervision (Zebrowitz & Lee, 1999), defence and nurturance (Alley 1983) in the caregiver.

Children have been demonstrated to have an awareness of facial cues in a similar way to adults. They can distinguish a child from an adult, based only on head shape, however, they have shown minimal ability to use this information to guide attributions of behavioural affordances (Montepare & McArthur, 1982, 1986).

In addition to having facial features which mimic those seen in infants, children with RSS are shorter than their peers, this alone may have a direct influence on how others perceive and treat them.

It is widely assumed that short children are disadvantaged (Law, 1987) with 56% of American physicians, in a 1996 survey, believing that short children would be advantaged with growth hormone therapy to increase their height (Cuttler *et al.*, 1996). Despite population studies of children with short stature revealing that short stature children differ little from their peers for self esteem and general development (Voss *et al.*, 1989; Downie *et al.*, 1997; Ulph, Betts, Mulligan & Stratford, 1994), adults still have lower expectations of short children. Tall male and female children have been found to be rated as more competent by adults than their short peers (Eisenberg, Roth, Bryniarski, Murray, 1984) and teachers report short children as less mature and have lower scholastic expectations of them than their taller peers (Wake, Coghlan & Hesketh, 2000). This again is a demonstration of overgeneralization, adults are making ability predictions based on a physical appearance, with those displaying the physical feature, short stature, of younger children being attributed the behavioural traits of younger children.

This research has three main aims. The first aim is to assess the effect of an RSS typical face shape on trait attributions; it is hypothesised that the RSS typical facial features will be rated higher for both infantile physical features and personality features. The second aim is to assess for an effect of height on the attribution of infantile physical and personality features. It is hypothesised that short stature will be attributed the highest level of infantile physical and personality features.

Chapter 5: Study 6: Russell Silver Syndrome: Effect of Face Shape and Height on Trait Attributions

The research has been split in to two sections. Section 1 reports data collected from an undergraduate population, while the second section reports data collected from a primary school (peer) population.

Study Aims

- Comparison of traits attributed to children with RSS typical facial features and control facial features by undergraduates and peers
- Comparison of trait attribution dependent on height
- Assessment of interaction between face shape and height for trait attribution.

Section 1 - Undergraduates

Method

Participants

120 young adults (59 males and 61 females) aged 18-32 (mean 21.05, SD 2.29), were recruited from within the School of Psychology, University of Birmingham and around the University of Birmingham campus.

Stimuli

Upper-body photographs were taken of four boys and four girls aged between 7 and 10 years. The four male pictures were digitally placed on to a blank background and made to appear as though they were standing behind a hedge. It was then possible to manipulate the height of one male, 3rd in line, in the picture relative to the others in the picture to create three height conditions, shorter, the same height, and taller, than the other pictured boys. In addition the face shape of the target male was manipulated, using Squirrelz morph, to create two face shape conditions, RSS typical and control. To create RSS typical facial features the top of the head was drawn out slightly and the chin in. In total, six conditions were created, RSS typical facial features short, average, and tall, and control facial features, short, average, and tall. The same procedure was repeated creating the six female picture stimuli. All pictures were presented in black and white to allow for photocopying. See appendix for stimuli.

Questionnaire

The questionnaire was devised to measure ten traits, four physical (attractive, baby faced, cute and physically strong) and six personality/behavioural (friendly, bossy, intelligent, mature, independent, and caring). The questionnaire was based on the questions used by Berry & McArthur (1985), in their research assessing the consequence of baby face features in adults. The questionnaire was presented on one A4 sheet, with a 7 point likert scale for each trait, participants were asked to indicate how much they felt the target child, in the photograph, had each of the traits, with 1 being 'very much' to 7 'not at all'. Participants were also asked to estimate the age of the target child.

Procedure

Participants were approached by a researcher either in the School of Psychology, University of Birmingham or around the University of Birmingham campus and were asked if they had time to complete a quick questionnaire. Brief instructions were provided for participants on a cover sheet along with a space to indicate their age and gender. Overleaf was one version of the male picture, with the target child indicated by a small star. Participants rated the target on each of the traits on the questionnaire, circling the point on the likert scale where they would place the target, and indicating their age estimate. This procedure was then repeated for the female picture. Picture presentation was counterbalanced so no combination of male and female conditions were always presented together.

Results

Kolmogorove Smirnov z analysis revealed that all data was normally distributed and box plot analysis revealed no outliers, therefore parametric analysis has been used throughout. Due to the large number of comparisons to be made a conservative alpha of 0.01 has been used.

Male Picture

A MANOVA was used to assess for the effects of face shape and height on the dependent variable of infantile physical appearance. There was no significant effect of face (RSS or control) on the combined Dependent Variable (DV) of infantile physical appearance ($F(4,112)=1.82, p=$), but a significant effect of height (short, average or tall) was found ($F(8,224)=2.29, p=0.023$). The

Chapter 5: Study 6: Russell Silver Syndrome: Effect of Face Shape and Height on Trait Attributions

interaction between face shape and height for physical appearance was not found to be significant ($F(8,224)=0.33, p=0.96$).

Further analysis was conducted for each individual DV for height, using a bon-ferroni adjusted alpha of 0.013 (0.05/4). This showed that the only physical trait found to be significantly affected by height was baby face ratings ($F(2,115)=10.59, p=0.005$). Bon ferroni post hoc revealed that short and average height conditions did not differ significantly for baby face ratings ($p=0.69$), nor did the average and tall conditions ($p=0.13$), but that short and tall conditions did differ significantly ($p=0.004$).

A second MANOVA was conducted to assess for the effects of face shape and height on the combined dependent variable of infantile personality. This revealed no significant effect of face (RSS or control) ($F(5,110)=0.87, p=0.50$), nor was there a significant effect of height (short, average or tall) on the DV infantile personality ($F(10, 222)=0.70, p=0.73$). The interaction between face shape and height was not found to be significant for personality ($F(10,222)=1.44, p=0.16$).

In addition to the main traits, participants were asked to estimate the age of the target boy in the picture. A 2 x 3 repeated measures ANOVA revealed there was no significant effect of face shape (RSS or Control) on the estimated age of the boy ($F(1,113)=2.06, p=0.015$) or of height (tall, average or short) ($F(2,113)=0.73, p=0.49$). The interaction between face shape and height was not found to be significant ($F(2,113)=1.49, p=0.23$).

Female picture

As with the male pictures, a MANOVA was used to assess for the effect of face shape and height on the combined dependent variable of infantile physical appearance. There was no significant effect of face shape (RSS or control) on the combined DV of infantile physical appearance ($F(4,110)=0.41, p=0.80$) but a significant effect of height (short, average or tall) on the DV was found ($F(8,220)=2.90, p=0.004$). A significant interaction between face shape and height was also found for infantile physical appearance ($F(8,220)=2.70, p=0.007$).

Analysis of each individual DV for height, using a bonferroni adjusted alpha level of 0.013, showed that height did not have a significant effect on any one of the DVs. Analysis of each individual DV for the interaction between face shape (RSS or control) and height (short, average or

tall), again using an adjusted alpha of 0.013, revealed a significant interaction for baby face ($F(2,113)=4.73, p=0.011$) and strength ($F(2,113)=5.18, p=0.007$). Interactions can be seen in graph 1 (baby face) and graph 2 (strength).

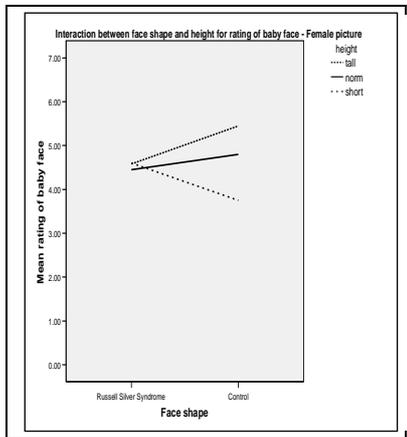


Figure 1: Interaction between face shape and height for baby face ratings on the female picture

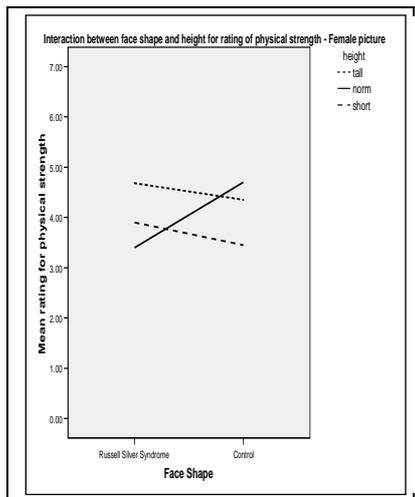


Figure 2: Interaction between face shape and height for strength ratings on the female picture

A second MANOVA was conducted for the combined DV of infantile personality. There was no significant effect of face (RSS or control) on the combined DV of personality ($F(5,108)=0.53, p=0.75$), nor was there a significant effect of height (short, average or tall) on personality ($F(10, 216)=1.10, p=0.36$). The interaction between height and face shape for personality was not found to be significant ($F(10,216)=1.03, p=0.42$).

Chapter 5: Study 6: Russell Silver Syndrome: Effect of Face Shape and Height on Trait Attributions

As with the male picture, estimated age of the target girl in the picture was compared using a 2 x 3 ANOVA. This revealed no significant effect of face shape on estimated age ($F(1, 111)=2.49$, $p=0.12$), though a significant effect of height was found ($F(2,111)=10.55$, $p<0.001$). A bon ferroni post hoc revealed that the tall condition were found to be rated as significantly older than both the average ($p<0.001$) and short ($p<0.001$) conditions, while the short and average conditions were not found to differ ($p=1.0$). The interaction between height and face shape was not found to be significant ($F(2,111)=0.71$, $p=0.49$).

Summary- Section 1

The main aims of this research were to assess the impact of short stature and RSS typical facial features, in children, on the attribution of infantile traits, physical and personality, and to assess for any significant interactions. Overall the findings were surprising in the lack of significant effects.

One of the main assumptions underlying the first hypothesis of this research, that children with RSS will be attributed more infantile physical and personality traits, is that the facial features seen in children with RSS are infantile. Baby faced children have previously been reported to be rated as physically weaker, socially submissive, naive, cute and warm (Berry & McArthur, 1985; Masip et al., 2004; McArthur & Apatow, 1983) with the effect being thought to be due to an overgeneralization of the traits of babies to those who display similar physical features (Berry & McArthur, 1985; Masip et al., 2004). It was predicted that as the features of RSS are in many ways similar to the facial features of babies, an RSS typical facial appearance would be attributed more infantile traits. This research did not find that adults rated males or females with RSS typical facial features, as physically different from those with control facial features, and more specifically it failed to find that they were rated as more baby faced. The expectation, therefore, that the RSS typical face would be attributed more different personality traits, was unlikely to be found.

It was possible that the target in the RSS typical condition was being seen as younger than in the control condition, and trait attributions were being made age appropriately, however a comparison of predicted age across face shape conditions was not significant for the male or female picture.

The effect of a child's stature on trait expectations of adults has also been previously investigated, with the general finding, that those with short stature would be expected to be at a

disadvantage, with parents and teachers having an expectation that short stature children are less competent (Eisenberg et al., 1984), less mature and less scholastically able than their taller peers (Wake et al., 2000).

This research found that although adults rated both the male and female pictures as physically different dependent on height, they were not found to differ on the dependent variable of personality according to height. Although adults in this research were recognising that there was something physically different they did not have different personality expectations dependent on height, which was a surprising finding in the light of previous research.

For the male picture there was not found to be an effect of height on predicted age, which indicates that the lack of effect of height on personality traits is unlikely to be due to age appropriate attributions being made. For the female picture however, an effect of height on age predictions was reported, with adults rating children in the tall picture as significantly older than the average or short conditions which were not found to differ significantly. In the case of the female picture, physical and personality trait attributions being made age appropriately can not be ruled out. In order to reduce the risk of this effect in further research it would be recommended that participants are told that all the girls in the photograph are the same age.

There were two surprising interactions between height and face shape for the female picture only, these were for baby face rating and physical strength. In the baby face condition the tall and average conditions were, as expected, rated as more baby faced than in the RSS than control condition, however in the short condition the opposite was found, with the control condition being rated as more baby faced. When graphical representations were analyzed it was revealed that this effect was small. The three groups, tall, average and short, were found to differ very little for the RSS typical face condition, but for the control condition the pattern was as expected, with the short condition being as the most baby faced and the tall condition the least baby faced. The second interaction was for physical strength. This again saw the expected pattern in two of the height conditions, tall and short, with the RSS typical facial condition being rated as physically weaker than the control condition, however, for the average height the reverse was found, with the RSS typical face condition being rated as physically stronger than the control condition. This finding was

surprising and difficult to explain. A potential cause for this effect could be that when height was not different between the target and other children in the picture, more attention was paid to other physical features, specifically face shape, and this was a better indicator of physical strength. If this was the case however, it would be expected that other traits would also have shown similar effects.

Section 2 - children

Participants

143 children (71 males, 72 females), aged 6-11 (mean 6.8, SD 1.05) were recruited from a Lancaster junior school. Parents of the children were given information about the study and the opportunity to opt their child out.

Stimuli

The same pictures as described in Study 1 were used.

Questionnaire

The same ten traits, four physical (attractive, baby face and physically strong, cute) and six personality (friendly, bossy, intelligent, mature, independent and caring) as used in section 1 were used with children. Responses were indicated using a pictorial likert scale, with a small circle indicating that they feel the target child would not display the trait “very much” and a large circle indicating they felt they would display the trait “a lot”.

Procedure

Children completed the study, with one of three researchers, in a quiet corridor outside their classroom during a normal school day. The age and gender of the child was taken and the nature of the study and of the scale, were briefly explained to the child. The child was then shown the first picture, and their attention was brought to the target as the one about which they must answer the questions. The researcher then asked the child to rate the target on each of the traits in turn, using the pictorial likert scale, and to estimate the age of the child in the picture. The researcher recorded the answers that each child gave. Each child saw one version of the male and one of the female pictures, with presentation pairs counter balanced as with the undergraduates.

Results

Male picture

A MANOVA was used to assess for the effects of face shape and height on the dependent variable of physical appearance. There was no significant effect of face (RSS or control) on the combined DV of physical appearance ($F(4,133)=0.54$, $p=0.71$) or significant effect of height (short, average or tall) on physical appearance ($F(8,266)=0.97$, $p=0.46$). The interaction between face shape and height for physical appearance was not found to be significant ($F(8, 266)=1.32$, $p=0.23$).

A second MANOVA was conducted to assess for the effects of face shape and height on the combined dependent variable of personality. This revealed no significant effect of face (RSS or control) ($F(5,132)=1.44$, $p=0.21$), nor was there a significant effect of height on the DV of personality ($F(10,264)=1.16$, $p=0.32$). The interaction between face shape and height was not found to be significant for personality ($F(10,264)= 0.72$, $p=0.70$).

Children were asked to estimate the age of the target boy, and estimates were compared using a 2 x 3 ANOVA. This revealed that there was no significant effect of face shape (RSS or control) on age estimates ($F(1,136)=0.18$, $p=0.67$), or of height (short, average or tall) on age estimates ($F(2,136)=0.93$, $p=0.40$). The interaction between face shape and height was not found to be significant ($F(2,136)=0.95$, $p=0.039$).

Female picture

A MANOVA was used to assess for the effects of face shape and height on the dependent variable of physical appearance. There was a significant effect of face (RSS or control) on the combined DV of physical appearance ($F(4,135)=4.60$, $p=0.002$), but no significant effect of height (short, average or tall) on physical appearance was found ($F(8,270)= 0.56$, $p=0.81$). The interaction between face shape and height for physical appearance was not found to be significant ($F(8, 270)= 1.49$, $p=0.16$).

Further analysis was conducted for each individual DV for face shape, using a bon-ferroni adjusted alpha of 0.013. This showed that the only physical feature found to be significantly affected by face shape was baby face ratings ($F(1,138)=13.54$, $p=<0.001$).

Chapter 5: Study 6: Russell Silver Syndrome: Effect of Face Shape and Height on Trait Attributions

A second MANOVA was conducted to assess for the effects of face shape and height on the combined dependent variable of personality. This revealed no significant effect of face (RSS or control) ($F(5,134)=0.57, p=0.72$), nor was there a significant effect of height on the DV personality ($F(10,264)=1.62, p=1.00$). The interaction between face shape and height was not found to be significant for personality ($F(10,264)=0.71, p=0.71$).

Estimated age of the target girl in the picture was compared using a 2 x 3 ANOVA. The analysis revealed no significant main effect of face shape (RSS or control) ($F(1,138)=1.37, p=0.025$), or of height (short, average or tall) ($F(2,138)=1.65, p=0.20$). The interaction between face shape and height for estimated age was not found to be significant ($F(2,138)=0.73, p=0.49$).

Summary

There is little research to date assessing how changes in facial features and height of children affect the trait attributions other children make. This research revealed no significant effect of face shape or height on trait attributions of the male picture. For the female picture a significant effect of face shape for infantile physical features was found. During testing it was noted that children often commented that the girl looked 'strange' and 'odd' in the RSS typical condition, showing an awareness that there were physical differences in that condition. Positively, despite noting that there was a physical difference between the two facial conditions, this did not impact on the personality traits which the children attributed. Height was not found to have an effect on the physical and personality trait attributions, for the female picture.

As with the adult data, children were asked to estimate the age of the child in the pictures and no effect of face shape or height was found for estimated age for either the male or female picture. It can be assumed that the lack of differences in personality trait attributions for both males and females, was not due to age appropriate attributions being made.

The findings here, with children, were to a certain extent expected. Children have previously been shown to have an awareness of facial cues (Montepare & McArthur, 1982), and here children showed an awareness of physical differences, for the female picture between the two facial conditions. Previous research has shown that despite an awareness of physical differences, children do not use

this information to guide trait affordances (Montepare & McArthur, 1982; 1986), again this was demonstrated in this research by the lack of difference between conditions for personality trait.

Discussion

Overall the findings from this research have been positive for children with RSS. Adults have shown that the RSS typical facial shape did affect their attribution of infantile traits physical or personality traits, in either the male or female conditions. While they did attribute more infantile physical traits dependent on height, it did not follow that they also attributed more infantile personality traits.

Children were shown to be minimally affected by the changes in face shape and height on their attribution of infantile features. While they did show that there was an effect of face shape on physical ratings for the female picture only, this did not impact on their attribution of personality traits.

This research suggests that children with RSS are unlikely to be treated differently by adults or peers, although there are restrictions to these findings. There is a possibility in this research that there were few significant findings as the children in the pictures were all seen as having the physical and personality traits at a 'ceiling level', all children are seen as having high levels of infantile traits, simply because they are children. It is thought this may be the case particularly with the male stimuli as many participants commented that the control picture was 'cute' and 'sweet'. It may be that the male chosen was demonstrating infantile traits at a ceiling level, and the changes could not make the child appear more infantile, this should have been assessed before the research was conducted and is a short fall of the research study.

The research conducted here was in a contrived situation, where people were actually asked to think about their trait attributions. A better understanding of how people react to children with RSS typical features and short stature would be achieved using observational measures, where you would get a natural reaction and would be able to measure real life responses, rather than the 'thought through' responses encouraged in this research.

Chapter 5: Study 6: Russell Silver Syndrome: Effect of Face Shape and Height on Trait Attributions

In the future it would be interesting to replicate this study with different populations, possibly parents or teachers, who have had a lot more contact with children of the age in the pictures; previous experience would be expected to affect the responses given. Undergraduates would be expected to have had little contact with 6-7 year olds, as a population.

Overall the findings from this research have been positive, and based on these findings it would not be expected that children with RSS features would be likely to be treated differently by others. These findings would also support the finding of Study 6 in this thesis, which found that children with RSS were not found to have lower self esteem than control children.

5.4 CHAPTER 5: DISCUSSION

The aim of this chapter was to investigate the psychosocial profile of children with RSS and this was approached in two ways. Firstly a direct analysis was made of how the self esteem of children with RSS differs from that of age matched control children. Following from this the body image attitude, height, weight and face shape, of RSS and control children were compared. The second study in this chapter aimed to assess how others perceived children with RSS typical features, short stature and a phenotypical 'babyish' face shape. It was believed that adults and peers would have different perceptions of children with RSS typical features, and this could in turn be impacting on how they would treat children with RSS, with the overall effect of an impacted self esteem.

The first surprising finding of this chapter was that the RSS children did not have lower self esteem than did control children, this effect was found to be true of both RSS children over the age of 8 years, and those below this age. Previous research had suggested that being short statured and being referred to growth clinics, as children with RSS are, would have a negative impact on self esteem (Kranzler et al., 2000; Bussbach et al., 1998). It was believed in the case of RSS this would be further impacted by being treated differently due to their baby like facial appearance.

RSS children were found to be shorter and lighter than control children, and while they did show an awareness and dissatisfaction with their height, they were found to see their weight as comparable to control children and showed no weight dissatisfaction. No effect of face shape was found, with the two groups, control and RSS seeing themselves as comparable on this factor. The finding that children with RSS were aware that they were short and were dissatisfied with their height could have suggested that they would also have lower self esteem than control children. That this was not found to be the case suggests that they are employing a self defence mechanism, possibly due to a large number receiving GHT which has been associated with increased self esteem (Boulton et al., 1991), or due to having a cause for their short stature in RSS.

Some gender differences in body image attitude were found, RSS males did not see themselves as shorter than controls, but their ideal height was taller than that of control children, possibly reflecting the fact that they were less comfortable choosing the socially undesirable short

picture. RSS females were however found to rate themselves as shorter than control children and less satisfied with their height. These findings were to be expected, as short stature is not seen as negative in females in the same way it is in males, as is evidenced by the smaller number of females referred to growth clinics (Grimberg et al., 2005; Kranzler et al., 2000).

The findings from Study 7, which investigated how others see children with RSS typical features, were also, on the whole, surprising. It had been expected that short stature and baby like facial features, as seen in RSS, would be attributed more infantile traits by adults and peers. While some effects of height were found in adult's ratings, the effects were restricted to the attribution of physical traits, and despite differences in physical ratings, this did not, in turn, affect personality trait attribution. In peers, very few effects of physical features on either physical trait ratings or personality trait ratings were found. This was in part to be expected, as although children have previously been found to be aware of physical differences, this has not been found to impact on their personality trait attribution (Montepare & McArthur, 1982; 1986).

Overall the findings from this chapter were very encouraging for children with RSS. The negatively impacted self esteem which had been expected, was not found. Children with RSS view themselves differently for height, but there appears to be a cognitive defence mechanism from this impacting their self esteem. They were not found to be unhappy with either their weight or face shape. The typical features of RSS were not found to be impacting on the perception of adults and peers of children with RSS. As this research suggests that RSS children are unlikely to be treated differently by others, it may have been expected that their self esteem would not have been affected.

CHAPTER 6

GENERAL DISCUSSION

6.1 Aims of the present thesis

As outlined in section 2.8, the overall aim of the current thesis was to understand better the cognitive, behavioural and psychosocial profile of children with RSS. The rationale for this research was that, although there is much ongoing research into what causes RSS and the physical effects of this condition, little is known about the children's psychological development. The present thesis aimed to address this deficit in knowledge, and further more to look for causes for any difficulties that were found in children with RSS.

Previous research into the psychological profile of children with RSS had been limited to overviews of their cognitive profile. Further to this existing research (Lai et al., 1994; Noeker & Wollman, 2004), the first aim of this thesis was to reassess and investigate the cognitive profile of children with RSS. An in depth investigation was made of the cognitive profile of children with RSS, in comparison to an age and gender matched control group, assessing for specific areas of cognitive dysfunction.

The second aim of this thesis was to investigate the behavioural profile of children with RSS, in response to anecdotal reports by parents and physicians that RSS children were displaying high levels of behavioural problems. The RSS group and control group were compared to assess for general behavioural problems, ADHD and ASD.

The final aim of this thesis was to assess the psychosocial profile of children with RSS. The self esteem and body image attitude of RSS children was investigated and as children with RSS have a physically different appearance to other children, the way that others perceive and treat children with RSS physical features was also looked at.

A summary of all the important findings from this thesis can be found in table 6.1, this can be used as a reference to guide the discussion

Table 6.1: Summary of findings from study 2, 3, 4 and 5

	Whole RSS v Control	RSS Male v Control Male	RSS Female v Control Female	<8 years RSS v <8 years control	> 8 years RSS v > 8 Years control	RSS ASD v RSS nonASD
Study 2 – The cognitive ability of children with Russell Silver Syndrome						
General Cognitive Ability	RSS < Control	-	-	RSS = Control	RSS < Control	
Spatial ability	-	-	-	-	RSS = Control	
Non-verbal ability	-	-	-	-	RSS = Control	
Verbal ability	-	-	-	-	RSS = Control	
Across cluster comparison	-	-	-	-	Spatial < Non-verbal < Verbal	
Recall of design (spatial cluster)	-	-	-	-	RSS < Control	
Recall of objects Immediate Verbal	-	-	-	-	RSS < Control	
Speed of Information Processing	-	-	-	-	RSS < Control	
Recall of Digits Forward	-	-	-	-	RSS < Control	
Birth weight significant confounding factor	-	-	-	-	Yes	
Gestational age significant confounding factor	-	-	-	-	Yes	
Study 3 – The incidence and description of behavioural problems and ADHD in Russell Silver Syndrome						
Total behavioural difficulties	RSS > Control	RSS > Control	RSS = Control	-	-	
Emotional Difficulties	RSS > Control	RSS = Control	RSS > Control	-	-	
Conduct Difficulties	RSS > Control	RSS = Control	RSS = Control	-	-	
Hyperactivity Difficulties	RSS > Control	RSS > Control	RSS = Control	-	-	
Peer Problems	RSS > Control	RSS > Control	RSS = Control	-	-	
Impact of behavioural difficulties	RSS > Control	RSS = Control	RSS = Control	-	-	
ADHD rating scale total score	RSS > Control	RSS > Control	RSS > Control	-	-	
ADHD rating scale hyperactivity/impulsivity	RSS > Control	RSS > Control	RSS = Control	-	-	
ADHD rating scale inattention	RSS > Control	RSS > Control	RSS > Control	-	-	
Birthweight as a confounding factor	No	-	-	-	-	-

Gestational age as a confounding factor	No	-	-	-	-	-
Study 4 – Autistic Spectrum Disorder and Russell Silver Syndrome: Incidence and risk factors						
SCQ Total Score	RSS > Control	-	-	-	-	
SCQ Communication difficulties	RSS > Control	-	-	-	-	
SCQ Repetitive behaviours	RSS > Control	-	-	-	-	
SCQ Social behaviours	RSS = Control	-	-	-	-	
Birthweight						RSS ASD < RSS no ASD
Gestational age						RSS ASD = RSS no ASD
Maternal age						RSS ASD = RSS no ASD
MatUPD7						RSS ASD = RSS no ASD
Asymmetry						RSS ASD = RSS no ASD
Facial features						RSS ASD = RSS no ASD
Study 5 – Self esteem and body image attitude in Russell Silver Syndrome						
Cognitive SE					RSS = Control	
Physical SE					RSS = Control	
Social SE					RSS = Control	
Maternal SE					RSS = Control	
Scholastic SE						RSS = Control
Social SE						RSS = Control
Athletic SE						RSS = Control
Physical SE						RSS = Control
Bheavioural SE						RSS = Control
Global Self Worth						RSS = Control
Actual height	RSS < Control	-				
Actual Weight	RSS < Control	-				
Perceived height	RSS < Control	RSS = Control	RSS < Control	RSS = Control	RSS < Control	-
Ideal height	RSS = Control	RSS > Control	RSS = Control	RSS = Control	RSS = Control	-
Height dissatisfaction	RSS < Control	-				
Perceived weight	RSS = Control	-				

Ideal weight	RSS = Control	RSS = Control	RSS = Control	RSS = Control	RSS = Control	-
Weight dissatisfaction	RSS < Control	RSS = Control	RSS < Control	RSS = Control	RSS = Control	-
Actual face shape	RSS = Control	RSS = Control	RSS < Control	RSS = Control	RSS < Control	-
Perceived face shape	RSS = Control	RSS = Control	RSS < Control	RSS = Control	RSS = Control	-
Face shape dissatisfaction	RSS = Control	RSS = Control	RSS = Control	RSS = Control	RSS = Control	-

Significant findings indicated in **Bold** text

The general discussion of this thesis will be presented in three sections to reflect the three aims of the thesis.

- The cognitive profile of children with RSS
- The behavioural profile of children with RSS
- The psychosocial profile of children with RSS.
- The overall profile of children with RSS, bringing together all the findings .

6.2 The cognitive profile of children with RSS

6.2.1 Hypotheses and Summary of Results

6.2.1.1 Comparison of the cognitive profile of RSS and controls

The first aim of this investigation was to compare the overall cognitive profile of RSS with a control group. It was hypothesised, based on previous research with RSS children (Lai et al., 1994; Noeker and Wollmann, 2004), and a systematic review of the long term consequences of children born SGA (Study 1), that children with RSS would display a significant General Cognitive Ability (GCA) deficit relative to the age matched control group. Study 2 of this thesis, with a large RSS group revealed that the GCA of the RSS group was significantly lower than that of the control group.

6.2.1.2 Effect of age on cognitive ability

A second aim of this section was to assess whether cognitive ability in RSS reduced with age. The trend in previous research, assessing the cognitive abilities of children with RSS, suggested that improved understanding and interventions with RSS, SGA and the associated post natal complications was having a positive impact on cognitive ability (Lai et al., 1994; Noeker & Wollmann, 2004). While the more recent research of Noeker & Wollman (2004) reported, deficit in the cognitive abilities of children with RSS relative to controls, the deficit reported was much smaller than that reported by Lai et al., (1994). In addition, while Lai et al., (1994) reported a correlation between head growth and IQ, with the possibility of both being caused by repeated hypoglycaemia, this was not reported by Noeker & Wollmann (2004), again suggesting that the incidence of hypoglycaemia and the consequences of this, had been reduced.

Previous research, with children born SGA (Study 1), had reported a cognitive deficit in older SGA children where one had not been detected at younger ages. Study 1 of this thesis concluded that this may be due to improved postnatal care and reduced adverse consequences. Alternatively, it was suggested that the effect of age was due to the greater demand of graphomotor skills and hand eye coordination in cognitive testing with older children. It has been shown that SGA children do display some difficulties in this area. This research hypothesised that children with RSS who took the school age battery of the BAS-II (>8 years) would have a significantly lower GCA than those who took the early years battery (< 8years) and that there would be a correlation between age and General Cognitive Ability (GCA).

Overall the GCA of children with RSS was not found to correlate with age, suggesting that the potential adverse postnatal consequences of being born SGA have been recognised, and treated, for a number of years, and no substantial improvements had been made in this time.

While this research did not confirm the hypothesis that younger RSS children would be able to achieve better GCA scores due to less physical and graphomotor demands of the task, this may be due to the fact that the youngest children that participated were five years old, and the cognitive test used for this age group still required a degree of motor accuracy and skill, previous research had only reported no deficit in cognitive testing with children of 3 years (Fattal-Valevski et al., 1997; Andersson et al., 1997; Markestad et al., 1997).

6.2.1.3 Deficit in specific areas of functioning?

The third aim, of this section, was to assess whether there was a specific area of functioning that the RSS children were displaying difficulties with. A review of research working with SGA children (Study 1), suggested that children born SGA at term may be reported as having a cognitive deficit as a result of difficulties in tasks with high grapho-motor skill and hand eye coordination demands. It was therefore hypothesised that RSS children, who are also born SGA at term, would have a significant deficit in the spatial tasks of the BAS-II relative to the verbal and non-verbal tasks, as these tasks were known to require high levels of hand eye coordination and graphomotor skills.

RSS children were not found to differ significantly from control children in any one specific area of functioning, verbal ability, non-verbal ability or spatial ability. A within group comparison

across areas of functioning, however, found that RSS children had a significant deficit in spatial ability relative to their verbal ability. Further comparisons of RSS and control groups on individual core and supplemental tasks of the BAS-II, showed that significant group differences were found on the recall of design task, recall of objects immediate, and recall of digits forward. All of these tasks have some similarity in the demand on working memory, further investigations in to the working memory of children with RSS would be needed in order to ascertain whether this is the cause of the cognitive difficulties that they are experiencing.

6.2.1.4 Effect of behavioural problems on cognitive ability

The final aim of this section was to assess the impact of behavioural problems, such as ADHD and ASD, on the cognitive ability of children with RSS. It was found that RSS children displayed more behavioural difficulties than did controls (Study 3), symptoms of ADHD were found to be greater in children with RSS than controls. It is known that ADHD can have a negative impact on academic achievement and qualifications (Biederman, 2005), and it was predicted that ADHD score would correlate negatively with GCA, this was not found to be the case. This may reflect however that GCA is not an appropriate measure of academic functioning; academic achievement may have been more accurate. Additionally, it can not be ruled out that this lack of correlation was due to only parental reports of ADHD symptoms being collected, teacher reports may give a more accurate reflection of school functioning.

ASD was also investigated in children with RSS, and it was revealed that there was a raised incidence of ASD in RSS (Study 4). It was predicted that those who were found to have RSS and ASD would have lower general cognitive abilities than the remainder of the RSS group. This research however found that the RSS ASD and RSS non-ASD groups were cognitively comparable.

6.2.1.5 Effect of birthweight and gestational age on cognitive ability

Previous research has indicated a relationship between reduced birth weight and lower cognitive ability (ref), and reduced gestational age and lower cognitive ability (ref). Both these factors were independently controlled for and the RSS and control groups were once again compared. When these factors were controlled, the RSS and control groups no longer differed significantly for

cognitive ability, indicating that both these factors have a significant impact on the fact that RSS children were found to have a lower cognitive ability.

6.2.2 Contribution of the present results to the understanding of the cognitive abilities of children with RSS

The present thesis aimed to investigate the cognitive abilities of children with RSS, with particular focus on the effect of age on cognitive abilities, and the overall profile of cognitive abilities in children with RSS.

Previous research had found that children with RSS were displaying cognitive abilities below that of controls (Lai et al., 1994; Noeker & Wollmann, 2004) and this research continued to reflect this finding.

The present findings suggest that children with RSS are having particular difficulties with spatial tasks, it was found that they were having particular difficulties with the tasks which require working memory, though further investigations would be needed of their memory specifically to look for patterns in this area and exclude the possibility of executive functioning difficulties. It would also be helpful to further investigate the graphomotor and fine motor skills in children with RSS as these too could be impacting on their performance on the cognitive testing.

Birthweight and gestational age were both found to be significant factors for the cognitive ability of children with RSS, this is an important finding, as it suggests that those children with RSS with the lowest birthweight and gestational age are at the greatest risk of long term cognitive complications.

6.3 The behavioural profile of children with RSS

6.3.1 Hypotheses and Results

6.3.1.1 Overall behavioural profile

The first aim of this section was to compile an overall behavioural profile of children with RSS. Previous research working with children born SGA (see Study 1), had revealed that SGA children are at an increased risk of symptoms of ADHD, but this is specific to being born SGA with post-natal complications (Robson & Cline, 1998). An investigation comparing the behavioural profile of the RSS group with that of an age and gender matched control group (Study 3), revealed that the

RSS group were displaying significantly more behavioural difficulties, than were control children, this was not found to be limited to symptoms of ADHD, but also more emotional difficulties, conduct difficulties, and peer problems.

6.3.1.2 Effect of gender on behavioural problems

Previous research has suggested that males are more likely to display externalising behavioural symptoms, than females (Biederman, 2002; Levy, 2005). It was therefore predicted in this research that there would be gender effects in the presentation of behavioural symptoms in children with RSS, with males reporting more externalising behaviours and females more internalising. Study 3 of this thesis, compared RSS males with control males, and RSS females with control females for behavioural problems. For their overall behaviour RSS females were only found to display significantly more emotional difficulties than were controls, while for males more hyperactivity, and peer problems were reported in RSS than controls. It was also revealed that RSS females were not reporting significantly more symptoms of hyperactivity/impulsivity (externalising) than control females (study 3), but they were displaying significantly more symptoms of inattention (internalising) than control females. RSS males however, were reporting both more hyperactivity/impulsivity and inattention than control males (study 3).

6.3.1.3 Effect of birth weight on behavioural

Being born with reduced birth measurements has previously been associated with increased attention difficulties (Hack et al., 2004; Indredavik et al., 2005; O’Keeffe et al., 2003; Mick et al., 2002; Elgen et al., 2004; Kelly et al., 2001), however, being born SGA at term, without additional complications (Indredavik et al., 2003; 2005) has not been associated with any adverse consequences. It was hypothesised that children with RSS would have been at risk of additional complications, due to poor weight gain and feeding problems, and therefore birth weight could be a mediatory factor in reported behavioural problems. Birth weight was found to be significantly correlated with ADHD score in this research (Study 3), however, when birth weight was controlled there continued to be a significant difference in the attention difficulties reported in the RSS and control groups, suggesting birth weight alone can not account for the raised incidence of ADHD found in children with RSS. However, birth weight alone can also not predict post natal complications, and further research would

require a better control of complications, possibly through the use of longitudinal research with children diagnosed with RSS, with access to medical records.

6.3.1.4 ASD in RSS

The second specific aim of this section was to assess the incidence of ASD in children with RSS, this was further to parent and physician reports of increased incidence of ASD in children with RSS. It was expected that significantly more children with RSS would receive a diagnosis of ASD than control group children, and that this would be at the high functioning end of the autistic spectrum. The research aimed to investigate the type of ASD, and to see if any one factor, e.g. birth weight, gestational age, RSS genetics, RSS symptom presentation, separated those with RSS that would receive a diagnosis from the remainder of the RSS group. The incidence of ASD found in children with RSS, was higher than the national average, with a conservative estimate of a 5 fold increase in the probability of RSS children having an ASD (Study 4). The RSS children with ASD reported in Study 4 were all high functioning, and as already reported in section 6.2.1.4, they were not found to differ cognitively from the remainder of the RSS group. Investigations to find a cause for why only some, and not all, RSS children were found to have ASD, revealed that the ASD group did not differ from the remainder of the group for any of the pre- and peri-natal insults previously associated with ASD including, birth weight (Larsson et al., 2005; Hultman et al., 2005), gestational age (Williams et al., 2007; Cryan et al., 1996) or increased maternal age (Williams et al., 2007; Glasson et al., 2004; Hultman et al., 2002; Kolevzon et al., 2007; Larsson et al., 2005). It was further hypothesised that those with RSS ASD would form a homogenous group for RSS symptom presentation, possibly suggesting a specific form of RSS. The RSS ASD and RSS non-ASD groups however did not differ significantly for RSS symptoms. Finally, it was hypothesised that the RSS-ASD groups all had the same genetic aberration, matUPD7 or 11p15 or neither. Only one RSS ASD child had been genetically assessed, and found positive for matUPD7, however, several of the RSS non-ASD group were also found positive for this genetic link. It remains however possible, that matUPD7 is important in the development of ASD in children with RSS.

6.3.2 Contribution of the present results to the understanding of the behavioural profile of RSS

Prior to this research, little was known about the behavioural profile of children with RSS, although it had been suggested in a brief meeting abstract that there was an increased incidence of ADHD (Bogdanov et al., 1995).

This research developed a better understanding of the potential behavioural problems that children with RSS may face, which were revealed as potentially quite extensive.

Previous research has suggested that having increased symptoms of ADHD is associated with increased behavioural difficulties in other areas of functioning (Biederman, 2005; Holowenko, 1999; Murphy et al., 2002). The overall profile of children with RSS in this research would suggest that they have many behavioural difficulties, though whether increased attention problems are the route cause of other behavioural problems reported can not be proven at this time from this research.

As ASD had previously not been investigated in RSS, the findings from this research offer the first assessment that there is an increased likelihood of having ASD in RSS. The awareness that RSS is a risk factor for ASD, whatever the cause, will lead to better awareness and detection in RSS children. There is a great need for further investigations in to the mechanism of ASD in RSS, as this research proved inconclusive. It is particularly important that the genetics of those that receive a diagnosis of RSS and ASD are investigated.

6.4 The psychosocial profile of children with RSS

6.4.1 Hypotheses and summary of results.

Section 3 of this thesis consists of two parts, the first investigated how children with RSS view themselves, and whether this impacts on their self esteem. The second part of this section looked at how others viewed children with RSS typical features, and whether this was likely to impact on how they treated them.

6.4.1.1 Russell Silver Syndrome and Self Esteem

Study 5 hypothesised that children with RSS would have lower self esteem than control children. Previous research has found that children with short stature are often thought to be at a disadvantage (Gilmour & Skuse, 1996; Clopper, 1994; Harper, 2000), and they are at an increased risk of psychosocial problems including low self esteem, low social competence, and social

difficulties (Visser-an Balen et al., 2006; Gordon et al., 1982; Sandberg et al., 1994; Stabler et al., 1998; Gilmour & Skuse, 1996). These effects have been found to be more acute in children that are referred to growth clinics for short stature treatment (Kranzler et al., 2000; Bussbach et al., 1998), as children with RSS are. In addition, having facial features that resemble those of a baby, as seen in RSS, has previously been found to be linked to being attributed more baby like traits (Zebrowitz & Motepare, 1992; Zebrowitz et al., 1993; Berry & McArthur, 1985), and this too could be impacting on the self esteem of children with RSS. Children with RSS were, however, not found to have a lower self esteem than were control children. This effect was found in both young RSS children (<8years), and older RSS children (>8years).

6.4.1.2 Russell Silver Syndrome and body image attitude

It was hypothesised that children with RSS would have a more negative body image attitude than control children, and specifically they would display dissatisfaction with their height, weight and face shape. Previous research has found that short stature is seen as a disadvantage (Gilmour & Skuse, 1996; Clopper, 1994; Harper, 2000), therefore it was expected that the RSS children would demonstrate more height dissatisfaction than did control children, as short stature is one of the main features of the syndrome. Overall the RSS children were found to be shorter, and rated themselves as shorter and more dissatisfied with their height. They were not, however, found to rate themselves as thinner, or more dissatisfied with their weight, despite being lighter, or more dissatisfied with their face shape than were control children. It is thought that the lack of effect for weight, may be due to the thin ideal in the UK; it was in fact found that the control children were less satisfied with their weight and wanted to be thinner.

6.4.1.3 Gender effects on body image attitude

The effects of gender on body image attitude were investigated. It has previously been found that short stature may be more of an issue in males, than in females, with a male bias in growth clinic referrals (Grimberg et al., 2005; Kranzler et al., 2000). It was therefore hypothesised that RSS males would display significantly more height dissatisfaction than RSS females, this was not found to be the case. In fact both males and females were found to show height dissatisfaction, although it was found that RSS males did not report being shorter than controls, while RSS females did, possibly

representing the fact that RSS males are less comfortable accepting that they were short. It was also found that RSS males' ideal height was greater than that of the control group.

For weight there were also expected to be gender differences. There is a greater drive to be thin in girls than in boys (Stice & Bierman, 2001), with males often wanting to increase their body weight through increased muscle bulk, it was therefore hypothesised, that RSS males would want to be bigger, while RSS females would be happy with their weight. What was found was that neither males or females were unhappy with their weight, and while there was a significant difference between weight satisfaction for females this was caused by control females wanting to be thinner.

6.4.1.4 Effect of height and face shape on how others view children with RSS

The final aim of this thesis was to assess the effect of the physical features of RSS, short stature and phenotypical face shape, on the way others, peers and adult, perceive children with RSS. It was hypothesised that as children with RSS have facial features with similarities to those seen in babies, and short stature, they would be attributed more infantile traits, as physical features are known to guide our expectations of others (Santos & Young, 2005; Masip et al., 2004; McArthur & Baron, 1983). The physical features of RSS were, however, found to have very little impact on the trait attributions of either children or adults. For adult ratings no effect of face shape was found, and where effect of height on trait attributions were reported, these were limited to physical traits, with no effect on their personality expectations. Children did not rate those with RSS features differently to control children, apart from rating a female with RSS typical facial features as more baby faced. This was not found to impact on how they rated them on any personality trait.

6.4.2 Contribution of the present results to the understanding of the psychosocial profile of RSS

The findings from this section are important in that they are specific to children with RSS, before this research was conducted only inferences could be made about the psychosocial profile based on research with idiopathic short stature populations and children with baby faced facial features, rather than the specific facial features seen in RSS.

It was surprising to discover that the self esteem of children with RSS did not differ significantly from that of a control group, this would have been expected as they are a referred short stature population, with the addition of different facial features. This finding highlights the importance

of looking at the effect of symptoms on individual diagnoses. It can be hypothesised that having a known organic cause for short stature, in this case RSS, was acting as a cognitive defence mechanism against the psychological effects of short stature and referral. The research findings used to guide expectations in this research was conducted only with those with idiopathic short stature.

It was positive on the whole, to discover that children with RSS are happy with their weight and face shape, although there does remain the possibility that this could have a negative impact in adulthood. RSS adults have been anecdotally reported to gain weight, and are often found to be heavier than their peers. As the UK has a thin ideal, it would be important to monitor body image satisfaction in RSS adults, to look for any long term effects of being very thin in childhood, for example unexpected weight gain in a child who has always been very slim may be more confusing and distressing, than in children who have always been larger.

Finally, this research does offer some findings about stature that are generalisable to the general population. While it had been expected that short children, male and female, would be attributed more infantile personality traits this was not found to be the case. It appears, in the case of RSS, that even though they are shorter than their peers, RSS children are unlikely to be treated differently to their peers because of this, or because of their different facial features. This too could be an explanation for the lack of difference in findings between the self esteem of RSS and control group children.

6.5 The overall profile of RSS

It would be useful to draw together an overall profile of children with RSS in order for parents and professionals to take away an expectation of the developmental profile of a particular child. For example, if they have a very low birth weight would you also expect low cognitive scores? It remains difficult in this research to effectively pull together an overall profile statistically due to the small sample size and need to use different scales with different age groups, however, a factor analysis was conducted for the results from the older RSS children (>8years). The scores included in the analysis were weight centile, height centile, birthweight, total SDQ score, total ADHD score, total SCQ score, global self worth and general cognitive ability score. It would have been useful to look how the different sub-scales of the scales used loaded using a factor analysis, however, this would

have been far too many factors for the analysis of such a small group of participants. 3 factors were revealed, the first included weight, height, birthweight and SDQ score, this suggests that more behavioural problems will be expected in children with lower physical measurements. The second factor included total ADHD score, total SCQ score and global self worth, this suggests, as was demonstrated in study 4, that self esteem is not affected by physical measurements, however, more hyperactivity and inattention, and social communication problems are likely to have a negative impact on self esteem. The final factor only included one score, general cognitive ability, which is independent of the other factors of RSS, although it must be remembered that birthweight has previously been shown to be a significant factor in the development of cognitive difficulties.

In summary, those with the lowest physical measurements are more likely to experience behavioural difficulties generally. Those children with RSS who have symptoms of ADHD or social communication difficulties are more likely to have lower self esteem. General cognitive ability was not found to correlate significantly to any one factor, though it has previously been shown that birthweight is important in the development of difficulties.

6.6 Limitations of the present thesis

6.6.1 Methodological issues

6.6.1.1 Experimental design

This thesis used a cross sectional design, with a wide age range. While this allowed for an investigation of the effect of time of the consequences of RSS, what it did not allow for directly was an analysis of the effect of increasing age on the consequences of RSS. A longitudinal design would have offered a better overview of the effects of time on children with RSS, however, this would have been impossible to conduct, within the present time frame.

6.6.1.2 Measures used

The first major drawback of the measures used in this thesis was the demographic questionnaire used. This was used to collect measurement data, such as birth weight, gestational age, current height and current weight. All data were parentally reported, and would have been more

accurate had it been collected either from medical records, or by the researcher at the time of testing, in the case of current measurements.

In addition, the remainder of the questionnaires were limited to parent reports only. It has previously been demonstrated with the ADHD rating scale-IV (DuPaul et al., 1998), that the most accurate assessment would be obtained from using a combination of parent and teacher reports (Power et al., 1998; Cohen et al., 1990). The researcher was aware of this drawback and attempts were made to extend the collection of data to include teacher reports, however only a very small number of parents were happy for teachers to be approached to participate in the research.

In Study 5 of this thesis, it would have been better to use one measure of self esteem for all ages, as this would have allowed for the effects of gender on self esteem to be assessed, however, it has been suggested that the constructs of self esteem differ for older and younger children (Harter & Pike, 1984) and therefore any findings would have lost integrity if age inappropriate measures had been used. Despite this limitation, previous research had been found where the two measures were used in conjunction as they were in this research study (Goodman et al., 1993).

6.6.1.3 Participants and recruitment

The age matching of RSS and control participants was very broad, and while this was controlled for as far as possible by using age norms available with scales (study 2, 3), there still remained a possibility of variability in scores being due to age, rather than an actual difference in scores due to group. However, the mean age of the groups throughout this research was never found to differ significantly.

It would have been preferable to have an SGA group as a second control group throughout the thesis, however recruitment of SGA children across the entire age range was very difficult. As many SGA children do not receive growth hormone or clinic follow up recruitment of this group was very difficult. A large number are followed up to school age, but beyond this age, unless they are receiving GHT, they are discharged from hospitals.

The age range of children that participated in this research was broad (5-16), this had to be the case in order to recruit a sufficiently large group of children with RSS to participate due to the rarity of the syndrome. While there were advantages to having such a broad age range, in that the impact of

passing time and improved post natal care could be assessed, there were also methodological issues as a consequence. This was particularly an issue in the study assessing cognitive ability, and that assessing psychosocial development. In both these cases, it was inappropriate to use the same measure with all age groups, and having to use age appropriate scales meant that the number of children in the younger and older groups was small.

It would have been good in this research to separate those with RSS according to their RSS genotype, this however was impossible at this time. A large number of children with RSS that participated had not been genetically screened for MatUPD7, and at the time of starting this research none had been screened for 11p15. There is a possibility in the future that these comparisons could be made retrospectively using the data collected here.

6.7 Implications of the present results

Despite the limitations of the present thesis, the findings here have very real application to children with RSS. Prior to this research there was practically no empirical evidence of the long term development of children with RSS, most parents were reliant on anecdotal reports of behavioural problems, and quickly outdated reviews of the cognitive abilities of children with RSS.

Having an awareness that there may be difficulties in specific areas of functioning for children with RSS, such as in tasks with a high grapho-motor demands, or hand eye coordination, may allow parents, and teachers, to put in to place systems to improve these skills. Equally, knowledge that, on the whole, children with RSS are performing around average, may be detrimental. Even within the group that participated in this research, there were cases where they were scoring below average and this could be due to the consequences of being born RSS and SGA. RSS should remain a risk factor for cognitive difficulties, as the specific experiences of each RSS child, such as repeated hypoglycaemia could be having an individual impact.

An awareness of increased ADHD in RSS children is also a useful finding for parents and teachers. As RSS can now be seen as a risk factor for increased attention difficulties, assessment could be routinely made. Early detection of these difficulties reduces the risk of children developing concurrent behavioural difficulties, or the attention difficulties impacting on long term academic development. Similarly, an awareness of an increased risk of ASD in children with RSS will allow for

earlier detection and better application of interventions, reducing the long term adverse consequences associated with ASD to a minimum.

Not all children with RSS are currently prescribed GHT, this is very much dependent on their height trajectory. The findings from study 6 was that receiving GHT, while potentially increasing actual height, did not increase self esteem, nor make children with RSS more positive about their height. GHT is a long term treatment with daily injections with, in some children, only small height gains. As short stature in this population does not appear to be having a negative impact on children's self esteem, it should not always be an automatic option for aesthetic reasons.

6.8 Future directions of research

While this research fulfilled its aims in creating a cognitive, behavioural and psychosocial profile of children with RSS, it also highlighted future directions in which the research could be taken.

Many parents, throughout the RSS group, reported that their child was experiencing speech and language difficulties and were often seeing speech and language therapists. In the future, it would be of benefit to assess what sort of speech and language problems RSS children were experiencing, looking for patterns and trends in the types of problems reported. Previous research had noted that there are often speech and language difficulties in children born SGA (Leitner et al., 2007), and it has been highlighted previously in research with children with RSS (Lai et al., 1994), though it remains un-investigated.

This research would have benefitted from having the genotype of all RSS participants, this would have allowed for assessment of psychological profiles specific to each genetic aberration. While this was impossible at the time of this research being conducted, as the majority of participants had not been genetically assessed, it may be possible to do these assessments using the data collected here retrospectively.

A final direction that this research could and should be taken in, is further investigations of the neuro-cognitive profile of children with RSS, specifically their fine motor skills and hand eye coordination, and also their executive functioning. It was proposed in this research that deficits found in spatial ability relative to verbal ability could be due to either of these factors, further, more in depth, investigations are essential to confirm or disprove this hypothesis.

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APPENDIX A

Cover letter and information pack for RSS parents

Dear Parent(s)/Guardian(s),

You and your child are being invited to take part in a research study currently being run by the University of Birmingham and Birmingham Children's Hospital on the behavioural and psychosocial issues (e.g. self esteem) that are shown by children with Russell Silver Syndrome (RSS), children Small for Gestational Age (SGA), and children of normal height (control group). We would be very grateful if you would consider participating in the study as a member of the RSS group. I have enclosed an information letter for you and one for your child about the study. These information sheets will explain what the study is about and what you will do if you take part. Please take the time to read it carefully in order to decide whether or not you would like for you and your child to participate. If you do decide to take part there are two consent forms enclosed for you to complete. One of these is for you to keep and one is for you to send back to me in the prepaid envelope provided.

Thank you for your time.

Yours faithfully,

Amy Barkham
Applied Developmental Post-Graduate Researcher

ASSESSING THE PSYCHOSOCIAL PROFILE AND BEHAVIOURAL PROFILE OF CHILDREN WITH RUSSELL SILVER SYNDROME IN COMPARISON TO CHILDREN THAT ARE SMALL FOR GESTATIONAL AGE AND CHILDREN OF NORMAL HEIGHT

Dear Parent(s)/Guardian(s),

You and your child are being invited to take part in a research study currently being run by Birmingham Children's Hospital and the University of Birmingham, on the behavioural and psychosocial issues (e.g. self esteem) that are shown by children Small for Gestational Age (SGA), children with Russell Silver Syndrome (RSS), and children of normal height (control group).

Russell-Silver Syndrome is a rare condition present at birth and is usually diagnosed in early childhood. It is characterised by poor growth demonstrated by low birth weight and short stature (a person significantly below the average height for a person of matched age and sex). Physical features are often seen and these include asymmetry in the body; a small triangular face with a small jaw, pointed chin, and a thin wide mouth; the little finger of each hand may be short and curve inwards. However, it is important to note that these children are unlikely to have all these features described.

Small for Gestational Age refers to when a baby is born with a weight that is inappropriately low for the duration of the pregnancy, for example, for a baby born at term this would be a birth-weight below 2.5kg.

The control group is a group of children who do not have growth problems. The purpose of this group is to serve as a baseline to compare the other two experimental groups of children who do have growth problems. This will ensure that the results we find are due to experimental conditions and not due to any other factors.

We would be very grateful if you would consider participating in the study as a **member of the Russell Silver Syndrome group**. Please take time to read the following information carefully, and discuss it with others if you wish. Contact us if there is anything that is not clear to you, or if you would like more information.

Thank you for reading this.

WHAT IS THE PURPOSE OF THIS STUDY?

The research is a publicly funded scientific investigation that has been requested by parents of children with RSS that are members of the Child Growth Foundation. When the study is completed the researcher will obtain a PhD in Applied Developmental Psychology. This study will compare the psychosocial and behavioural profile of children who have RSS, with children that are SGA, and children of normal height. We will attempt to identify what the typical psychosocial issues are for these children, and the range of behaviours that tend to be shown by these groups. We will also attempt to identify the causes.

WHAT WILL I HAVE TO DO?

If you participate in this study, all you will have to do is fill in some questionnaires about your child. Altogether these should take approximately 25 minutes to complete. One questionnaire will be sent to be filled out by your child, you are allowed to assist if necessary. This will take approximately 5 minutes to complete. One questionnaire will also ask some information about your self. This should take approximately 5 minutes to complete. We will also need to make some visits to carry out some of the assessments of your child, which will be planned at your convenience. These assessments are not invasive and will require your child to complete activities such as copying designs, giving definitions of words, and answering questions about themselves. This should take about an hour and a half to do. We may also wish to videotape some of your child's behaviour. These videos will be kept in a secure room and will be destroyed **2011**¹ (three years after the study is completed) using a bulk eraser. Erased videos will then be disposed of safely following a procedure recommended by the University of Birmingham. The study is completely safe and is by no means invasive. You and your child will not be putting yourself at any potential risk by participating.

WILL MY TAKING PART IN THIS STUDY BE KEPT CONFIDENTIAL?

All information which is collected about you and your child during the course of the research will remain completely confidential. All information will be kept in a secure room and will be destroyed in **2011**.

DO I HAVE TO TAKE PART?

You do not have to participate in this research. However, if you do decide to participate you may keep this information pack, and send back a completed consent form. If you decide to participate then you are still free to withdraw at any time without giving a reason.

ARE THERE ANY BENEFITS?

There will be no direct benefits to research participants. However, this study will help us to understand any problems in the psychosocial functioning of these children, and any behaviours that may be problematic. This will mean that we can help health professionals, parents, and teachers to be aware of these issues and help them to develop good coping strategies.

WHO ELSE IS TAKING PART?

We require large numbers of children with RSS and their parents to complete the study, so that we can compare these results with those from parents of SGA children and control children. Parents of children who have RSS, or are SGA will be members

of the Child Growth Foundation, or will attend the Growth Clinic at Birmingham Children's Hospital, Addenbrookes Hospital Cambridge, or the Royal Hospital for Sick Children, Glasgow.

WHAT IF SOMETHING GOES WRONG?

Nothing should go wrong with the study, however, if for any reason you feel that you have a cause for concern about the research you may discuss these with the chief researcher, **Amy Barkham** and/or her supervisor, Dr. Gillian Harris, who is a Paediatric Clinical Psychologist (details on next page).

If for any reason you decide to withdraw from the study, you are free to do so at any time without giving any reason and your future care will not be affected.

Alternatively, you may contact **Dr. Gillian Harris** at the following address:

Dr. Gillian Harris

WHAT HAPPENS NOW IF I DECIDE TO TAKE PART?

Please complete the two enclosed consent forms and questionnaire. One consent form is for you to keep and the other to be returned along with the questionnaire, in the prepaid envelope provided.

For further questionnaires and assessments, you will be contacted within a few months. Please write your name, address and, daytime telephone number (if possible), on the questionnaires.

Thank you very much for your time.

Yours Faithfully,

Amy Barkham
PhD Student

The University of Birmingham agrees to compensate against claims for damages, loss, and costs, and expenses incurred as a result of bodily injury to persons &/or damage to material property arising out of any negligent act or omission of the chief researcher during the period of the study.

CONSENT FORM

ASSESSING THE PSYCHOSOCIAL PROFILE AND BEHAVIOURAL PROFILE OF CHILDREN WITH RUSSELL SILVER SYNDROME IN COMPARISON TO CHILDREN THAT ARE SMALL FOR GESTATIONAL AGE AND CHILDREN OF NORMAL HEIGHT

Name of Researcher: **Amy Barkham**

Please initial box

- I confirm that I have read and understand the information sheet (**26/10/05, version 4.0**) for the above study and have had opportunity to ask questions.
- I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.
- I understand that documents including video material, relating to me/my child will not be identifiable by name and will be kept confidential
- I agree to take part in the above study

Name of child Signature (if applicable) Date

Name of parent Signature Date

1 for the participant; 1 for researcher

Recruitment Centre No:_____; Study No:____; Participant Group No:____ Participant No_____

APPENDIX B

Information pack RSS >10 years

INFORMATION SHEET

CHILDREN WITH RUSSELL SILVER SYNDROME, CHILDREN SMALL FOR GESTATIONAL AGE AND CHILDREN OF NORMAL HEIGHT

You and your parent(s)/guardian(s) are being invited to take part in a research study that is being run by the University of Birmingham and Birmingham Children's Hospital. The study is about 2 groups of children with growth problems. The study is about 2 groups of children with growth problems. One group will have Russell Silver Syndrome like you, and one group will be Small for Gestational Age. The study is also about groups of children without growth problems. We would be very pleased if you would like to take part in the study as **a member of the group of children with Russell Silver Syndrome**. Please take time to read the information in this letter carefully. If you do not understand anything you can ask your parents for help.

Thank you very much for reading this.

WHAT IS THIS STUDY ABOUT?

This study will look at the differences between children with Russell Silver Syndrome, children Small for Gestational Age and children without growth problems.

WHAT WILL I HAVE TO DO?

If you decide that you would like to take part in this study, we will send your parent(s) and you some questionnaires to complete. Some of these will be for your parent(s) and you some questionnaires to complete. Some of these will be for your parents to do, and one will be for you to do. If you find them hard then your parent(s) may help you. The questionnaire for you should take you about 5 minutes. We will also need to come and visit you to do some activities such as copying designs, giving meanings to words and answering some questions about yourself. This will take just over an hour. We may want to video you as well. No one but the people doing the research will see the videos and when the study is over the videos will be destroyed.

WHAT WILL HAPPEN TO THE INFORMATION?

No one will know who has filled in the forms, and your name will not be told to anyone. All the information will be used to write a report on the study, but no one will know who took part in it.

DO I HAVE TO TAKE PART?

You do not have to take part.

WILL THIS STUDY HELP ME?

The study will not help you. But, this study will help us to understand any problems children in these groups may have. This will mean that we can help doctors, parents, and teachers to be aware of these problems, and help them to find good ways of coping.

WHO ELSE IS TAKING PART?

We need lots of parents and their children who do and do not have growth problems to take part.

WHAT IF SOMETHING GOES WRONG?

Nothing should go wrong with the study. But if for any reason you decide you do not want to take part in the study anymore, you may stop at any time.

WHAT HAPPENS AT THE END OF THE STUDY?

You can get a summary of the findings of the study if you would like one.

WHAT IF I HAVE MORE QUESTIONS?

Please ask your parent(s)/guardian(s) if there is anything that you do not understand. If you do not know the answer then you can ask them to write or phone **Amy Barkham** at the following address:

Amy Barkham,

WHAT HAPPENS NOW IF I DECIDE TO TAKE PART?

Tell your parent(s)/guardian(s) that you are happy to take part, and they will have the forms to fill in.

Thank you very much!!

Amy Shayle
PhD Student

APPENDIX C

Information pack RSS < 10 years

INFORMATION SHEET

A PROJECT ABOUT CHILDREN WITH GROWTH PROBLEMS AND CHILDREN WITHOUT GROWTH PROBLEMS

You and your parent(s)/guardian(s) are being invited to take part in a project that is being run by the University of Birmingham and Birmingham Children's Hospital. The project is about children like you who have problems growing, and also about children who do not have growth problems. We would be very pleased if you would like to take part in the study **as a member of the group of children with Russell Silver Syndrome**. Please take time to read the information in this letter carefully with your parent(s)/guardian(s). You can ask as many questions as you like.

Thank you very much for reading this.

WHAT IS THIS STUDY ABOUT?

This study will look at the differences between children with growth problems and children without growth problems.

WHAT WILL I HAVE TO DO?

If you decide that you would like to take part in this study, we will send your parent(s), and you some questionnaires to do. Some of these will be for your parents to complete, and one will be for you to do. If you find them hard then your parent(s) may help you. The questionnaire for you should take about 5 minutes. We will also need to come and visit you to do some activities such as copying pictures, saying what words mean, and answering some questions about yourself. This will take just over an hour to do. We may want to video you as well. No one but the people doing the research will see the videos, and 3 years after the study is over the videos will be destroyed.

WHAT WILL HAPPEN TO THE INFORMATION?

No one will know who has filled in the forms, and your name will not be told to anyone. All the information will be used to write a report on the study, but no one will know who took part in it.

DO I HAVE TO TAKE PART?

You do not have to take part.

WILL THIS PROJECT HELP ME?

The study will not help you. But, this project will help us to understand any problems children in these groups may have. This will mean that we can help doctors, parents, and teachers to be aware of these problems, and help them to find good ways of coping.

WHO ELSE IS TAKING PART?

We need lots of parents and children like you who have growth problems to take part, and also parents and children who do not have growth problems to take part.

WHAT IF SOMETHING GOES WRONG?

Nothing should go wrong with the study. But if for any reason you do not want to take part in the study anymore, you may stop at any time.

WHAT HAPPENS AT THE END OF THE PROJECT

You can get a summary of the findings of the project if you would like one.

WHAT IF I HAVE MORE QUESTIONS?

Please ask your parent(s)/guardian(s) if there is anything that you do not understand. If they do not know the answer then you can ask them to write or phone **Amy Barkham** at the following address:

Amy Barkham,

WHAT HAPPENS NOW IF I DECIDE TO TAKE PART?

Tell your parent(s)/guardian(s) that you are happy to take part, and they will have the forms to fill in.

Thank you very much!!

Amy Barkham
PhD Student

APPENDIX D

Cover letter and information pack for SGA/IUGR parents

Dear Parent(s)/Guardian(s),

You and your child are being invited to take part in a research study currently being run by the University of Birmingham and Birmingham Children's Hospital on the behavioural and psychosocial issues (e.g. self esteem) that are shown by children Small for Gestational Age (SGA), including those with Intra Uterine Growth Restriction (IUGR), children with Russell Silver Syndrome (RSS) and children of normal height (control group). We would be very grateful if you would consider participating in the study as a member of the SGA/IUGR group. I have enclosed an information letter for you and one for your child about the study. These information sheets will explain what the study is about and what you will do if you take part. Please take the time to read it carefully in order to decide whether or not you would like for you and your child to participate. If you do decide to take part there are two consent forms enclosed for you to complete. One of these is for you to keep and one is for you to send back to me in the prepaid envelope provided.

Thank you for your time.

Yours faithfully,

Amy Barkham
Applied Developmental Post-Graduate Researcher

ASSESSING THE PSYCHOSOCIAL PROFILE AND BEHAVIOURAL PROFILE OF CHILDREN WITH RUSSELL SILVER SYNDROME IN COMPARISON TO CHILDREN THAT ARE SMALL FOR GESTATIONAL AGE AND CHILDREN OF NORMAL HEIGHT

Dear Parent(s)/Guardian(s),

You and your child are being invited to take part in a research study currently being run by Birmingham Children's Hospital and the University of Birmingham, on the behavioural and psychosocial issues (e.g. self esteem) that are shown by children Small for Gestational Age (SGA), children with Russell Silver Syndrome (RSS), and children of normal height (control group).

Small for Gestational Age refers to when a baby is born with a weight that is inappropriately low for the duration of the pregnancy, for example, for a baby born at term this would be a birth-weight below 2.5kg.

Russell-Silver Syndrome is a rare condition present at birth and is usually diagnosed in early childhood. It is characterised by poor growth demonstrated by low birth weight and short stature (a person significantly below the average height for a person of matched age and sex). Physical features are often seen and these include asymmetry in the body; a small triangular face with a small jaw, pointed chin, and a thin wide mouth; the little finger of each hand may be short and curve inwards. However, it is important to note that these children are unlikely to have all these features described.

The control group is a group of children who do not have growth problems. The purpose of this group is to serve as a baseline to compare the other two experimental groups of children who do have growth problems. This will ensure that the results we find are due to experimental conditions and not due to any other factors.

We would be very grateful if you would consider participating in the study as a **member of the Small for Gestational Age (inc. Intra Uterine Growth Restriction) group**. Please take time to read the following information carefully, and discuss it with others if you wish. Contact us if there is anything that is not clear to you, or if you would like more information.

Thank you for reading this.

WHAT IS THE PURPOSE OF THIS STUDY?

The research is a publicly funded scientific investigation that has been requested by parents of children with RSS that are members of the Child Growth Foundation. When the study is completed the researcher will obtain a PhD in Applied Developmental Psychology. This study will compare the psychosocial and behavioural profile of children who have RSS, with children that are SGA, and children of normal height. We will attempt to identify what the typical psychosocial issues are for these children, and the range of behaviours that tend to be shown by these groups. We will also attempt to identify the causes.

WHAT WILL I HAVE TO DO?

If you participate in this study, all you will have to do is fill in some questionnaires about your child. Altogether these should take approximately 25 minutes to complete. One questionnaire will be sent to be filled out by your child, you are allowed to assist if necessary. This will take approximately 5 minutes to complete. One questionnaire will also ask some information about your self. This should take approximately 5 minutes to complete. We will also need to make some visits to carry out some of the assessments of your child, which will be planned at your convenience. These assessments are not invasive and will require your child to complete activities such as copying designs, giving definitions of words, and answering questions about themselves. This should take about an hour and a half to do. We may also wish to videotape some of your child's behaviour. These videos will be kept in a secure room and will be destroyed **2011**¹ (three years after the study is completed) using a bulk eraser. Erased videos will then be disposed of safely following a procedure recommended by the University of Birmingham. The study is completely safe and is by no means invasive. You and your child will not be putting yourself at any potential risk by participating.

WILL MY TAKING PART IN THIS STUDY BE KEPT CONFIDENTIAL?

All information which is collected about you and your child during the course of the research will remain completely confidential. All information will be kept in a secure room and will be destroyed in **2011**.

DO I HAVE TO TAKE PART?

You do not have to participate in this research. However, if you do decide to participate you may keep this information pack, and send back a completed consent form. If you decide to participate then you are still free to withdraw at any time without giving a reason.

ARE THERE ANY BENEFITS?

There will be no direct benefits to research participants. However, this study will help us to understand any problems in the psychosocial functioning of these children, and any behaviours that may be problematic. This will mean that we can help health professionals, parents, and teachers to be aware of these issues and help them to develop good coping strategies.

WHO ELSE IS TAKING PART?

We require large numbers of children born SGA and their parents to complete the study, so that we can compare these results with those from parents of RSS children and control children. Parents of children who have RSS, or are SGA will be members

of the Child Growth Foundation, or will attend the Growth Clinic at Birmingham Children's Hospital, Addenbrookes Hospital Cambridge, or the Royal Hospital for Sick Children, Glasgow.

WHAT IF SOMETHING GOES WRONG?

Nothing should go wrong with the study, however, if for any reason you feel that you have a cause for concern about the research you may discuss these with the chief researcher, **Amy Barkham** and/or her supervisor, Dr. Gillian Harris, who is a Paediatric Clinical Psychologist (details on next page).

If for any reason you decide to withdraw from the study, you are free to do so at any time without giving any reason and your future care will not be affected.

Alternatively, you may contact **Dr. Gillian Harris** at the following address:

Dr. Gillian Harris

WHAT HAPPENS NOW IF I DECIDE TO TAKE PART?

Please complete the two enclosed consent forms and questionnaire. One consent form is for you to keep and the other to be returned along with the questionnaire, in the prepaid envelope provided.

For further questionnaires and assessments, you will be contacted within a few months. Please write your name, address and, daytime telephone number (if possible), on the questionnaires.

Thank you very much for your time.

Yours Faithfully,

Amy Barkham
PhD Student

The University of Birmingham agrees to compensate against claims for damages, loss, and costs, and expenses incurred as a result of bodily injury to persons &/or damage to material property arising out of any negligent act or omission of the chief researcher during the period of the study.

CONSENT FORM

ASSESSING THE PSYCHOSOCIAL PROFILE AND BEHAVIOURAL PROFILE OF CHILDREN WITH RUSSELL SILVER SYNDROME IN COMPARISON TO CHILDREN THAT ARE SMALL FOR GESTATIONAL AGE AND CHILDREN OF NORMAL HEIGHT

Name of Researcher: **Amy Barkham**

Please initial box

- I confirm that I have read and understand the information sheet (**26/10/05, version 4.0**) for the above study and have had opportunity to ask questions.
- I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.
- I understand that documents including video material, relating to me/my child will not be identifiable by name and will be kept confidential
- I agree to take part in the above study

Name of child

Signature (if applicable)

Date

Name of parent

Signature

Date

1 for the participant; 1 for researcher

Recruitment Centre No: _____; Study No: _____; Participant Group No: _____ Participant No _____

CONSENT FORM

ASSESSING THE PSYCHOSOCIAL PROFILE AND BEHAVIOURAL PROFILE OF CHILDREN WITH RUSSELL SILVER SYNDROME IN COMPARISON TO CHILDREN THAT ARE SMALL OR GESTATIONAL AGE AND CHILDREN OF NORMAL HEIGHT

Name of Researcher: **Amy Barkham**

Please initial box

- I confirm that I have read and understand the information sheet (**26/10/05, version 4.0**) for the above study and have had opportunity to ask questions.
- I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.
- I understand that documents including video material, relating to me/my child will not be identifiable by name and will be kept confidential
- I agree to take part in the above study

Name of child Signature (if applicable) Date

Name of parent Signature Date

1 for the participant; 1 for researcher

Recruitment Centre No:_____; Study No:____; Participant Group No:____ Participant No_____

APPENDIX E

Information pack SGA/IUGR > 10 years

INFORMATION SHEET

CHILDREN SMALL FOR GESTATIONAL AGE, CHILDREN WITH RUSSELL SILVER SYNDROME AND CHILDREN OF NORMAL HEIGHT

You and your parent(s)/guardian(s) are being invited to take part in a research study that is being run by the University of Birmingham and Birmingham Children's Hospital. The study is about 2 groups of children with growth problems. The study is about 2 groups of children with growth problems. One group will have Russell Silver Syndrome like you, and one group will be Small for Gestational Age. The study is also about groups of children without growth problems. We would be very pleased if you would like to take part in the study as **a member of the group of children who are Small for Gestational Age**. Please take time to read the information in this letter carefully. If you do not understand anything you can ask your parents for help.

Thank you very much for reading this.

WHAT IS THIS STUDY ABOUT?

This study will look at the differences between children Small for Gestational Age, children with Russell Silver Syndrome and children without growth problems.

WHAT WILL I HAVE TO DO?

If you decide that you would like to take part in this study, we will send your parent(s) and you some questionnaires to complete. Some of these will be for your parent(s) and you some questionnaires to complete. Some of these will be for your parents to do, and one will be for you to do. If you find them hard then your parent(s) may help you. The questionnaire for you should take you about 5 minutes. We will also need to come and visit you to do some activities such as copying designs, giving meanings to words and answering some questions about yourself. This will take just over an hour. We may want to video you as well. No one but the people doing the research will see the videos and when the study is over the videos will be destroyed.

WHAT WILL HAPPEN TO THE INFORMATION?

No one will know who has filled in the forms, and your name will not be told to anyone. All the information will be used to write a report on the study, but no one will know who took part in it.

DO I HAVE TO TAKE PART?

You do not have to take part.

WILL THIS STUDY HELP ME?

The study will not help you. But, this study will help us to understand any problems children in these groups may have. This will mean that we can help doctors, parents, and teachers to be aware of these problems, and help them to find good ways of coping.

WHO ELSE IS TAKING PART?

We need lots of parents and their children who do and do not have growth problems to take part.

WHAT IF SOMETHING GOES WRONG?

Nothing should go wrong with the study. But if for any reason you decide you do not want to take part in the study anymore, you may stop at any time.

WHAT HAPPENS AT THE END OF THE STUDY?

You can get a summary of the findings of the study if you would like one.

WHAT IF I HAVE MORE QUESTIONS?

Please ask your parent(s)/guardian(s) if there is anything that you do not understand. If you do not know the answer then you can ask them to write or phone **Amy Barkham** at the following address:

Amy Barkham

WHAT HAPPENS NOW IF I DECIDE TO TAKE PART?

Tell your parent(s)/guardian(s) that you are happy to take part, and they will have the forms to fill in.

Thank you very much!!

Amy Shayle
PhD Student

APPENDIX F

Information pack SGA/IUGR < 10 years

INFORMATION SHEET

A PROJECT ABOUT CHILDREN WITH GROWTH PROBLEMS AND CHILDREN WITHOUT GROWTH PROBLEMS

You and your parent(s)/guardian(s) are being invited to take part in a project that is being run by the University of Birmingham and Birmingham Children's Hospital. The project is about children like you who have problems growing, and also about children who do not have growth problems. We would be very pleased if you would like to take part in the study **as a member of the group of children Small for Gestational Age**. Please take time to read the information in this letter carefully with your parent(s)/guardian(s). You can ask as many questions as you like.

Thank you very much for reading this.

WHAT IS THIS STUDY ABOUT?

This study will look at the differences between children with growth problems and children without growth problems.

WHAT WILL I HAVE TO DO?

If you decide that you would like to take part in this study, we will send your parent(s), and you some questionnaires to do. Some of these will be for your parents to complete, and one will be for you to do. If you find them hard then your parent(s) may help you. The questionnaire for you should take about 5 minutes. We will also need to come and visit you to do some activities such as copying pictures, saying what words mean, and answering some questions about yourself. This will take just over an hour to do. We may want to video you as well. No one but the people doing the research will see the videos, and 3 years after the study is over the videos will be destroyed.

WHAT WILL HAPPEN TO THE INFORMATION?

No one will know who has filled in the forms, and your name will not be told to anyone. All the information will be used to write a report on the study, but no one will know who took part in it.

DO I HAVE TO TAKE PART?

You do not have to take part.

WILL THIS PROJECT HELP ME?

The study will not help you. But, this project will help us to understand any problems children in these groups may have. This will mean that we can help doctors, parents, and teachers to be aware of these problems, and help them to find good ways of coping.

WHO ELSE IS TAKING PART?

We need lots of parents and children like you who are Small for Gestational Age to take part, and also parents and their children who have Russell Silver Syndrome to

take part, and also parents and their children who do not have growth problems to take part.

WHAT IF SOMETHING GOES WRONG?

Nothing should go wrong with the study. But if for any reason you do not want to take part in the study anymore, you may stop at any time.

WHAT HAPPENS AT THE END OF THE PROJECT

You can get a summary of the findings of the project if you would like one.

WHAT IF I HAVE MORE QUESTIONS?

Please ask your parent(s)/guardian(s) if there is anything that you do not understand. If they do not know the answer then you can ask them to write or phone **Amy Barkham** at the following address:

Amy Barkham

WHAT HAPPENS NOW IF I DECIDE TO TAKE PART?

Tell your parent(s)/guardian(s) that you are happy to take part, and they will have the forms to fill in.

Thank you very much!!

Amy Barkham
PhD Student

APPENDIX G

Head teacher information pack

Dear (name of head teacher),

You, parents, and children from your school are being invited to take part in a research study currently being run by the University of Birmingham and Birmingham Children's Hospital on the behavioural and psychosocial issues (e.g. self esteem) that are shown by children Small for Gestational Age (SGA), children with Russell Silver Syndrome (RSS), and children of normal height (control group). We would be very grateful if you would consider allowing children and their parents from your school to participate in the study as members of the control group. I have enclosed an information letter for you about the study. This information letter will explain what the study is about and what you will do if you take part. I have also enclosed the sheets that would be sent out to parents and children. Please take the time to read these letters carefully in order to decide whether or not you would like for your school to participate. If you do decide to take part there are two consent forms enclosed for you to complete. One of these is for you to keep and one is for you to send back to me in the prepaid envelope provided.

Thank you for your time.

Yours faithfully,

Amy Barkham
Applied Developmental Post-Graduate Researcher

ASSESSING THE PSYCHOSOCIAL PROFILE AND BEHAVIOURAL PROFILE OF CHILDREN WITH RUSSELL SILVER SYNDROME IN COMPARISON TO CHILDREN THAT ARE SMALL FOR GESTATIONAL AGE AND CHILDREN OF NORMAL HEIGHT

Dear <name of head teacher>,

You, parents and children from your school are being invited to take part in a research study currently being run by Birmingham Children's Hospital and the University of Birmingham, on the behavioural and psychosocial issues (e.g. self esteem) that are shown by children Small for Gestational Age (SGA), children with Russell Silver Syndrome (RSS), and children of normal height (control group).

The control group is a group of children who do not have growth problems. The purpose of this group is to serve as a baseline to compare the other two experimental groups of children who do have growth problems. This will ensure that the results we find are due to experimental conditions and not due to any other factors.

Russell-Silver Syndrome is a rare condition present at birth and is usually diagnosed in early childhood. It is characterised by poor growth demonstrated by low birth weight and short stature (a person significantly below the average height for a person of matched age and sex). Physical features are often seen and these include asymmetry in the body; a small triangular face with a small jaw, pointed chin, and a thin wide mouth; the little finger of each hand may be short and curve inwards. However, it is important to note that these children are unlikely to have all these features described.

Small for Gestational Age refers to when a baby is born with a weight that is inappropriately low for the duration of the pregnancy, for example, for a baby born at term this would be a birth-weight below 2.5kg.

We would be very grateful if you would consider allowing children and their parents from your school to participate in the study **as members of the control group**. The following information in this letter will tell you about what the aims of the study are and what it will involve. Please contact us if there is anything that is not clear to you, or if you would like more information.

Thank you for reading this.

WHAT IS THE PURPOSE OF THIS STUDY?

This study will compare the psychosocial and behavioural profile of children who have RSS, with children that are Small for Gestational Age (SGA) , and children of normal height. We will attempt to identify what the typical psychosocial issues are for these children, and the range of behaviours that tend to be shown by these groups. We will also attempt to identify the causes.

DOES MY SCHOOL HAVE TO TAKE PART?

It is up to you to decide whether or not children from your school may be contacted to participate. If you decide for your school to participate you may keep this information pack, and send back a completed consent form. We will then send you information packs and consent forms to supply for parents and children. I will include an example of this information pack for you to view. It will then be the decision of the children's parent(s)/guardian(s) whether or not they wish to participate.

WHAT WILL I HAVE TO DO?

If you decide that your school will participate in this study, all you will be asked to do is to supply information sheets and consent forms to parents and children asking for them to take part. If parents and children decide to participate in this study they will have to complete the consent form and send it back to the researcher. Then all they will have to do is fill in a series of questionnaires. Most questionnaires will be for parents to fill in about their child. Some questionnaires will also be sent to be filled out by the child where parents are allowed to assist them if necessary. One questionnaire will also ask some information about parents. We will also need to make some visits to carry out some of the assessments of the children, which will be planned to the parent's convenience. We may also wish to videotape some of the children's behaviours. These will only be viewed by the researchers and will be destroyed in **2011**¹ (three years after the study is completed, with a bulk eraser. Erased videos will then be disposed of safely following a procedure recommended by the University of Birmingham. The study is completely safe is by no means invasive.

ARE THERE ANY BENEFITS?

There will be no direct benefits to the participants. However, this study will help us to understand any problems in the psychosocial functioning of these children, and any behaviours that may be problematic. This will mean that we can help health professionals, parents, and teachers to be aware of these issues, and help them to develop good coping strategies.

WILL DATA COLLECTED IN THIS STUDY BE KEPT CONFIDENTIAL?

All information which is collected during the course of the research will remain completely confidential. All information will be kept in a secure room and will be destroyed in **2011**.

WHAT IF I DO NOT WANT TO TAKE PART?

You are under no obligation to participate in this study.

WHO ELSE IS TAKING PART?

We require large numbers of control children and their parents to complete the study, so that we can compare these results with those from parents of children with RSS and those SGA. Parents of children who have RSS, or are SGA, will be members of the Child Growth Foundation, or will attend the Growth Clinic at Birmingham Children's Hospital or Cambridge Children's Hospital.

WHAT IF SOMETHING GOES WRONG?

Nothing should go wrong with the study. However, if for any reason you, parents or children feel that you have a cause for concern about the research you may discuss these with the chief researcher. **Amy Barkham** and/or her supervisor, Dr Gillian Harris, who is a paediatric Clinical Psychologist (details on next page).

If for any reason parents and children decide to withdraw from the study, they are free to do so at any time without giving any reason and your future care will not be affected.

WHAT HAPPENS AT THE END OF THE STUDY?

You will receive a summary of the findings, and also any advice that you may require.

WHO HAS REVIEWED THIS STUDY?

This study has been reviewed by West Midlands Multi-Centre Research Ethics Committee

WHAT IF I HAVE MORE QUESTIONS?

If you have any other questions then feel free to contact **Amy Barkham** at the following address

Amy Barkham

Alternatively, you may contact **Dr. Gillian Harris** at the following address:

Dr. Gillian Harris

WHAT HAPPENS NOW IF I DECIDE TO TAKE PART?

Please complete the two enclosed consent forms. One consent form is for you to keep and the other to be returned, in the prepaid envelope provided.

You will be sent information packs and consent forms to distribute to parents and children within a few months.

Thank you very much for your time.

Yours Faithfully,

Amy Barkham
PhD Student

The University of Birmingham agrees to compensate against claims for damages, loss, and costs, and expenses incurred as a result of bodily injury to persons &/or damage to material property arising out of any negligent act or omission of the chief researcher during the period of the study.

CONSENT FORM

ASSESSING THE PSYCHOSOCIAL PROFILE AND BEHAVIOURAL PROFILE OF CHILDREN WITH RUSSELL SILVER SYNDROME IN COMPARISON TO CHILDREN THAT ARE SMALL OR GESTATIONAL AGE AND CHILDREN OF NORMAL HEIGHT

Name of Researcher: **Amy Barkham**

Please initial box

1. I confirm that I have read and understand the information sheet (**26/10/2005, version 4.0**) for the above study and have had the opportunity to ask questions.

2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.

3. I agree to allow pupils from my school to be contacted to take part in the above study.

Name of Head Teacher

Signature (if applicable)

Date

Name of Researcher

Signature

Date

1 for the participant; 1 for researcher

Recruitment Centre No: _____; Study No: _____; Participant Group No: _____ Participant No _____

CONSENT FORM

ASSESSING THE PSYCHOSOCIAL PROFILE AND BEHAVIOURAL PROFILE OF CHILDREN WITH RUSSELL SILVER SYNDROME IN COMPARISON TO CHILDREN THAT ARE SMALL FOR GESTATIONAL AGE AND CHILDREN OF NORMAL HEIGHT

Name of Researcher: **Amy Barkham**

Please initial box

- 4. I confirm that I have read and understand the information sheet (26/10/2005, **version 4.0**) for the above study and have had the opportunity to ask questions.
- 5. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.
- 6. I agree to allow pupils from my school to be contacted to take part in the above study.

Name of Head Teacher Signature (if applicable) Date

Name of Researcher Signature Date

1 for the participant; 1 for researcher
Recruitment Centre No:_____; Study No:____; Participant Group No:____ Participant No:____

APPENDIX H

Cover letter and information pack control parents

Dear Parent/Guardian,

My name is Amy Barkham, I am a postgraduate researcher at the University of Birmingham. I am writing to invite you to become involved in the research I am currently conducting which is being run by the University of Birmingham and Birmingham Children's Hospital.

The research is looking on to the behavioural and psychosocial issues (e.g. self esteem) that are shown by children of normal height (control group), children with Russell Silver Syndrome (RSS), and children born Small for Gestational Age (SGA). We would be very grateful if you would consider participating in the study as a member of the control group. I have enclosed an information letter for you about the disorders we are looking at and the study as a whole. These information sheets will explain what the study is about and what you will do if you take part. Please take the time to read it carefully in order to decide whether or not you would like for you and your child to participate.

If you do decide to take part there are two consent forms enclosed for you to complete. One of these is for you to keep and one is for you to send back to me in the prepaid envelope provided along with the participation questionnaire enclosed.

I hope to hear from you soon, thank you for your time.

Yours faithfully,

Amy Barkham
Applied Developmental Post-Graduate Researcher

ASSESSING THE PSYCHOSOCIAL PROFILE AND BEHAVIOURAL PROFILE OF CHILDREN WITH RUSSELL SILVER SYNDROME IN COMPARISON TO CHILDREN THAT ARE SMALL FOR GESTATIONAL AGE AND CHILDREN OF NORMAL HEIGHT

Dear Parent(s)/Guardian(s),

You and your child are being invited to take part in a research study currently being run by Birmingham Children's Hospital and the University of Birmingham, on the behavioural and psychosocial issues (e.g. self esteem) that are shown by children of normal height, children born Small for Gestational Age (SGA) and children with Russell Silver Syndrome (RSS).

The control group is a group of children who do not have growth problems. The purpose of this group is to serve as a baseline to compare the other two experimental groups of children who do have growth problems. This will ensure that the results we find are due to experimental conditions and not due to any other factors.

Russell-Silver Syndrome is a rare condition present at birth and is usually diagnosed in early childhood. It is characterised by poor growth demonstrated by low birth weight and short stature (a person significantly below the average height for a person of matched age and sex). Physical features are often seen and these include asymmetry in the body; a small triangular face with a small jaw, pointed chin, and a thin wide mouth; the little finger of each hand may be short and curve inwards. However, it is important to note that these children are unlikely to have all these features described.

Small for Gestational Age refers to when a baby is born with a weight that is inappropriately low for the duration of the pregnancy, for example, for a baby born at term this would be a birth-weight below 2.5kg.

We would be very grateful if you would consider participating in the study as a **member of the Control group**. Please take time to read the following information carefully, and discuss it with others if you wish. Contact us if there is anything that is not clear to you, or if you would like more information.

Thank you for reading this.

WHAT IS THE PURPOSE OF THIS STUDY?

The research is a publicly funded scientific investigation that has been requested by parents of children with RSS that are members of the Child Growth Foundation. When the study is completed the researcher will obtain a PhD in Applied Developmental Psychology. This study will compare the psychosocial and behavioural profile of children who have RSS, with children that are SGA, and children of normal height. We will attempt to identify what the typical psychosocial issues are for these children, and the range of behaviours that tend to be shown by these groups. We will also attempt to identify the causes.

WHAT WILL I HAVE TO DO?

If you participate in this study, all you will have to do is fill in some questionnaires about your child. Altogether these should take approximately 25 minutes to complete. One questionnaire will be sent to be filled out by your child, you are allowed to assist if necessary. This will take approximately 5 minutes to complete. One questionnaire will also ask some information about your self. This should take approximately 5 minutes to complete. We will also need to make some visits to carry out some of the assessments of your child, which will be planned at your convenience. These assessments are not invasive and will require your child to complete activities such as copying designs, giving definitions of words, and answering questions about themselves. This should take about an hour and a half to do. We may also wish to videotape some of your child's behaviour. These videos will be kept in a secure room and will be destroyed **2011**¹ (three years after the study is completed) using a bulk eraser. Erased videos will then be disposed of safely following a procedure recommended by the University of Birmingham. The study is completely safe and is by no means invasive. You and your child will not be putting yourself at any potential risk by participating.

WILL MY TAKING PART IN THIS STUDY BE KEPT CONFIDENTIAL?

All information which is collected about you and your child during the course of the research will remain completely confidential. All information will be kept in a secure room and will be destroyed in **2011**.

DO I HAVE TO TAKE PART?

You do not have to participate in this research. However, if you do decide to participate you may keep this information pack, and send back a completed consent form. If you decide to participate then you are still free to withdraw at any time without giving a reason.

ARE THERE ANY BENEFITS?

There will be no direct benefits to research participants. However, this study will help us to understand any problems in the psychosocial functioning of these children, and any behaviours that may be problematic. This will mean that we can help health professionals, parents, and teachers to be aware of these issues and help them to develop good coping strategies.

WHO ELSE IS TAKING PART?

We require large numbers of control children and their parents to complete the study, so that we can compare these results with those from parents of SGA children and RSS children. Parents of children who have RSS, or are SGA will be members of the Child Growth Foundation, or will attend the Growth Clinic at Birmingham Children's Hospital, Addenbrookes Hospital Cambridge, or the Royal Hospital for Sick Children, Glasgow.

WHAT IF SOMETHING GOES WRONG?

Nothing should go wrong with the study, however, if for any reason you feel that you have a cause for concern about the research you may discuss these with the chief researcher, **Amy Barkham** and/or her supervisor, Dr. Gillian Harris, who is a Paediatric Clinical Psychologist (details on next page).

If for any reason you decide to withdraw from the study, you are free to do so at any time without giving any reason and your future care will not be affected. Alternatively, you may contact **Dr. Gillian Harris** at the following address:

Dr. Gillian Harris

WHAT HAPPENS NOW IF I DECIDE TO TAKE PART?

Please complete the two enclosed consent forms and questionnaire. One consent form is for you to keep and the other to be returned along with the questionnaire, in the prepaid envelope provided.

For further questionnaires and assessments, you will be contacted within a few months. Please write your name, address and, daytime telephone number (if possible), on the questionnaires.

Thank you very much for your time.

Yours Faithfully,

Amy Barkham
PhD Student

The University of Birmingham agrees to compensate against claims for damages, loss, and costs, and expenses incurred as a result of bodily injury to persons &/or damage to material property arising out of any negligent act or omission of the chief researcher during the period of the study.

CONSENT FORM

ASSESSING THE PSYCHOSOCIAL PROFILE AND BEHAVIOURAL PROFILE OF CHILDREN WITH RUSSELL SILVER SYNDROME IN COMPARISON TO CHILDREN THAT ARE SMALL OR GESTATIONAL AGE AND CHILDREN OF NORMAL HEIGHT

Name of Researcher: **Amy Barkham**

Please initial box

- I confirm that I have read and understand the information sheet (26/10/05, **version 4.0**) for the above study and have had opportunity to ask questions.
- I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.
- I understand that documents including video material, relating to me/my child will not be identifiable by name and will be kept confidential
- I agree to take part in the above study

Name of child Signature (if applicable) Date

Name of parent Signature Date

1 for the participant; 1 for researcher
Recruitment Centre No:_____; Study No:____; Participant Group No:____ Participant No_____

CONSENT FORM

ASSESSING THE PSYCHOSOCIAL PROFILE AND BEHAVIOURAL PROFILE OF CHILDREN WITH RUSSELL SILVER SYNDROME IN COMPARISON TO CHILDREN THAT ARE SMALLF OR GESTATIONAL AGE AND CHILDREN OF NORMAL HEIGHT

Name of Researcher: **Amy Barkham**

Please initial box

- I confirm that I have read and understand the information sheet (**26/10/05, version 4.0**) for the above study and have had opportunity to ask questions.
- I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.
- I understand that documents including video material, relating to me/my child will not be identifiable by name and will be kept confidential
- I agree to take part in the above study

Name of child Signature (if applicable) Date

Name of parent Signature Date

1 for the participant; 1 for researcher
Recruitment Centre No:_____; Study No:____; Participant Group No:____ Participant No_____

APPENDIX I

Information pack control > 10 years

INFORMATION SHEET

CHILDREN WITH RUSSELL SILVER SYNDROME, CHILDREN SMALL FOR GESTATIONAL AGE AND CHILDREN OF NORMAL HEIGHT

You and your parent(s)/guardian(s) are being invited to take part in a research study that is being run by the University of Birmingham and Birmingham Children's Hospital. The study is about 2 groups of children with growth problems. The study is about 2 groups of children with growth problems. One group will have Russell Silver Syndrome like you, and one group will be Small for Gestational Age. The study is also about groups of children without growth problems. We would be very pleased if you would like to take part in the study as **a member of the group of children without growth problems**. Please take time to read the information in this letter carefully. If you do not understand anything you can ask your parents for help.

Thank you very much for reading this.

WHAT IS THIS STUDY ABOUT?

This study will look at the differences between children without growth problems, children with Russell Silver Syndrome and born children Small for Gestational Age.

WHAT WILL I HAVE TO DO?

If you decide that you would like to take part in this study, we will send your parent(s) and you some questionnaires to complete. Some of these will be for your parent(s) and you some questionnaires to complete. Some of these will be for your parents to do, and one will be for you to do. If you find them hard then your parent(s) may help you. The questionnaire for you should take you about 5 minutes. We will also need to come and visit you to do some activities such as copying designs, giving meanings to words and answering some questions about yourself. This will take just over an hour. We may want to video you as well. No one but the people doing the research will see the videos and when the study is over the videos will be destroyed.

WHAT WILL HAPPEN TO THE INFORMATION?

No one will know who has filled in the forms, and your name will not be told to anyone. All the information will be used to write a report on the study, but no one will know who took part in it.

DO I HAVE TO TAKE PART?

You do not have to take part.

WILL THIS STUDY HELP ME?

The study will not help you. But, this study will help us to understand any problems children in these groups may have. This will mean that we can help doctors, parents, and teachers to be aware of these problems, and help them to find good ways of coping.

WHO ELSE IS TAKING PART?

We need lots of parents and their children who do and do not have growth problems to take part.

WHAT IF SOMETHING GOES WRONG?

Nothing should go wrong with the study. But if for any reason you decide you do not want to take part in the study anymore, you may stop at any time.

WHAT HAPPENS AT THE END OF THE STUDY?

You can get a summary of the findings of the study if you would like one.

WHAT IF I HAVE MORE QUESTIONS?

Please ask your parent(s)/guardian(s) if there is anything that you do not understand. If you do not know the answer then you can ask them to write or phone **Amy Barkham** at the following address:

Amy Barkham

WHAT HAPPENS NOW IF I DECIDE TO TAKE PART?

Tell your parent(s)/guardian(s) that you are happy to take part, and they will have the forms to fill in.

Thank you very much!!

Amy Shayle
PhD Student

APPENDIX J

Information pack control <10 years

INFORMATION SHEET

A PROJECT ABOUT CHILDREN WITH GROWTH PROBLEMS AND CHILDREN WITHOUT GROWTH PROBLEMS

You and your parent(s)/guardian(s) are being invited to take part in a project that is being run by the University of Birmingham and Birmingham Children's Hospital. The project is about children like you who have problems growing, and also about children who do not have growth problems. We would be very pleased if you would like to take part in the study **as a member of the group of children without growth problems**. Please take time to read the information in this letter carefully with your parent(s)/guardian(s). You can ask as many questions as you like.

Thank you very much for reading this.

WHAT IS THIS STUDY ABOUT?

This study will look at the differences between children with growth problems and children without growth problems.

WHAT WILL I HAVE TO DO?

If you decide that you would like to take part in this study, we will send your parent(s), and you some questionnaires to do. Some of these will be for your parents to complete, and one will be for you to do. If you find them hard then your parent(s) may help you. The questionnaire for you should take about 5 minutes. We will also need to come and visit you to do some activities such as copying pictures, saying what words mean, and answering some questions about yourself. This will take just over an hour to do. We may want to video you as well. No one but the people doing the research will see the videos, and 3 years after the study is over the videos will be destroyed.

WHAT WILL HAPPEN TO THE INFORMATION?

No one will know who has filled in the forms, and your name will not be told to anyone. All the information will be used to write a report on the study, but no one will know who took part in it.

DO I HAVE TO TAKE PART?

You do not have to take part.

WILL THIS PROJECT HELP ME?

The study will not help you. But, this project will help us to understand any problems children in these groups may have. This will mean that we can help doctors, parents, and teachers to be aware of these problems, and help them to find good ways of coping.

WHO ELSE IS TAKING PART?

We need lots of parents and children like you who have growth problems to take part, and also parents and children who do not have growth problems to take part.

WHAT IF SOMETHING GOES WRONG?

Nothing should go wrong with the study. But if for any reason you do not want to take part in the study anymore, you may stop at any time.

WHAT HAPPENS AT THE END OF THE PROJECT

You can get a summary of the findings of the project if you would like one.

WHAT IF I HAVE MORE QUESTIONS?

Please ask your parent(s)/guardian(s) if there is anything that you do not understand. If they do not know the answer then you can ask them to write or phone **Amy Barkham** at the following address:

Amy Barkham

WHAT HAPPENS NOW IF I DECIDE TO TAKE PART?

Tell your parent(s)/guardian(s) that you are happy to take part, and they will have the forms to fill in.

Thank you very much!!

Amy Barkham
PhD Student

APPENDIX K

Recruitment flyer



RESEARCH PARTICIPANTS WANTED

SCHOOL OF PSYCHOLOGY

We are currently running a study in the school of Psychology with children who are small for date babies, who continue to be short for their age.

We would like to compare these children with a **CONTROL GROUP** of children born with birth weight within the normal range and of average height.

- **Is your child aged 5 -16 years?**
- **Was their birth weight greater than 2500g (5.5lbs)?**
- **Is their height now comparable to their friends of the same age?**

If the answer is If the answer is **YES** to the questions above we would like to hear from you!

**ALL PARTICIPANTS WILL RECEIVE A £5
WATERSTONES VOUCHER**

To request an information pack please contact
AMY BARKHAM

APPENDIX L

Extended Strengths and Difficulties Questionnaire (ESDQ)

APPENDIX M

ADHD Rating Scale IV: Home Version

APPENDIX N

Social Communication Questionnaire : Lifetime Edition (SCQ)

APPENDIX O

Pictorial Scale of Perceived Self Confidence and Social Acceptance
for young children (PSPSCSA)

APPENDIX P

Self Perception Profile for Children (SPPC)

APPENDIX Q

Body image attitude stimuli, taken from Body Image Perception and attitude scale (BIPAS) and face shape stimuli

APPENDIX R

Parental Questionnaire

Parental Questionnaire

Name of child _____

Gender _____

Date of Birth _____

Home Address

Contact Telephone Number _____

Child's birth length _____ cm

Height now _____ cm

Height at 5 years _____ cm

Child's birth weight _____ Kgs

Weight now _____ Kgs

Weight at 5 years _____ Kgs

Child's head circumference at birth (if known) _____ cm

Is your child currently taking medication? Yes _____ No _____

If yes, please give the name of the medication, frequency given and reason for the medication. If your child is on growth hormone therapy please indicate how long they have been receiving treatment.

Has your child been in hospital in the last 12 months? Yes _____ No _____

If yes, how many times, for how long, and for what reason?

Has your child been seen by a speech and language therapist, occupational therapist, physiotherapist, orthodontist, optician in the last year?

Yes _____ No _____

If yes, whom has your child been seeing, and why have they been seeing them?

Has your child been seen by a specialist paediatrician (e.g. gastroenterologist), except for an endocrinologist in the past year?

Yes _____ No _____

If yes, who has your child seen and why?

At school does your child have a Statement of Special Needs, or any other special help?

Yes _____ No _____

If yes, please give details.

Did your child ever display excessive sweating as a baby? Yes ____ No ____

If yes, was it worse at a particular time of day? Yes ____ No ____

If yes, when?

Has your child ever been assessed as hypoglycaemic(low blood sugar)?

Yes ____ No ____

If so, at what age, and was any treatment prescribed?

Does your child have body asymmetry? Yes ____ No ____

Does your child have any unusual facial characteristics? Yes ____ No ____

If yes, please give details

Parental characteristics

Mother

Date of birth _____

Height _____

Occupation _____

Highest level of education

No formal qualifications _____

GCSE's/O-Levels _____

A-Levels _____

Undergraduate Degree _____

Postgraduate Degree _____

Father
Date of birth _____
Height _____
Occupation _____
Highest level of education

No formal qualifications _____
GCSE's/O-Levels _____
A-Levels _____
Undergraduate Degree _____
Postgraduate Degree _____

Was your child born prematurely? Yes ___ No ___
If yes, at how many weeks? _____

Does your child have any siblings? Yes ___ No ___
If yes, please could you give details of how many, whether they are older or younger and what sex they are.

Has your child ever been tube fed? Yes ___ No ___
Please give details.

Has your child been assessed for and found to have the uniparental disomy of chromosome 7 associated with RSS?
Yes ___ No ___ Never been assessed ___

APPENDIX S

Information for Study 6

November 2007

Parents / Carers of _____

Mr Guest has kindly given permission for me to conduct research in your child's school and I am writing to give you the opportunity to withdraw your consent. The study concerns Russell Silvers Syndrome (RSS). Children with this condition show characteristic facial features, with a large head tapering to a small jaw, giving their heads a triangular appearance. The purpose of the study is to understand how children perceive these facial features. Previous studies have found that adults perceive RSS faces differently to normal faces.

WHAT DOES THE STUDY INVOLVE?

My colleague or I will show your child photographs of children with or without the facial features characteristic of RSS. Your child will be asked to rate the face on a number of scales, for example friendliness and bossiness, and asked to estimate the age of the child. This will be repeated with 11 further photographs. All tasks will take place within school time and should take no longer than 10 minutes. If, for any reason, your child appears bored, does not talk, or indicates in any other way that he or she does not wish to participate, he/she will be able to return to his/her regular study or play.

WILL MY DETAILS BE KEPT CONFIDENTIAL?

Responses will be documented for later analysis. However, your child will remain anonymous and only my supervisor and I will have access to the questionnaire forms, which will be kept at a secure place. The forms will be labelled with a code, not with a name. All data will be destroyed in 2011.

ARE THERE ANY BENEFITS ?

There will be no direct benefits to participants. However, this study will help us to understand any problems in the psychosocial functioning of children with RSS, and any behaviours that may be problematic. This will mean we can help health professionals, parents and teachers to be aware of these issues, and help them to develop good coping strategies.

WHAT DO I DO NEXT?

If you are willing to allow your child to participate, you need not take any further action. However, if you wish your child **not** to take part, please complete the enclosed opt out forms. The First is to be returned to the school and the second is for you to cut out and keep. If you do not return the completed opt out form it will be assumed that you are happy for your child to participate.

I would appreciate it very much if you would help me with my study. In any case, I thank you for your consideration of this request. Do not hesitate to contact me or my postgraduate researcher if you have any questions.

THANK YOU VERY MUCH FOR YOUR TIME.

Yours sincerely
Danielle Fuller
Email :drf506@bham.ac.uk, Tel: 07835435702

For further details please contact-
Amy Barkham (Post graduate researcher, University of Birmingham)
Email: AXB242@bham.ac.uk, Tel: 01214143507

OPT OUT FORM
(Schools copy)

Study Investigating Others' Cognitions of Children with Russell Silvers Syndrome in Comparison to Controls.

If you would prefer your child **not** to participate in the study on perceptions of Russell Silvers syndrome faces, please sign the permission slip below and return it to your child's school within one week of receiving this letter.

I prefer that my child, {child's name} _____, does not participate in the study on perceptions of Russell Silvers syndrome faces.

Parent's (or guardian's) signature _____

Date _____



OPT OUT FORM
(parents copy)

Study Investigating Others' Cognitions of Children with Russell Silvers Syndrome in Comparison to Controls.

If you would prefer your child **not** to participate in the study on perceptions of Russell Silvers syndrome faces, please sign the permission slip below and return it to your child's school within one week of receiving this letter.

I prefer that my child, {child's name} _____, does not participate in the study on perceptions of Russell Silvers syndrome faces.

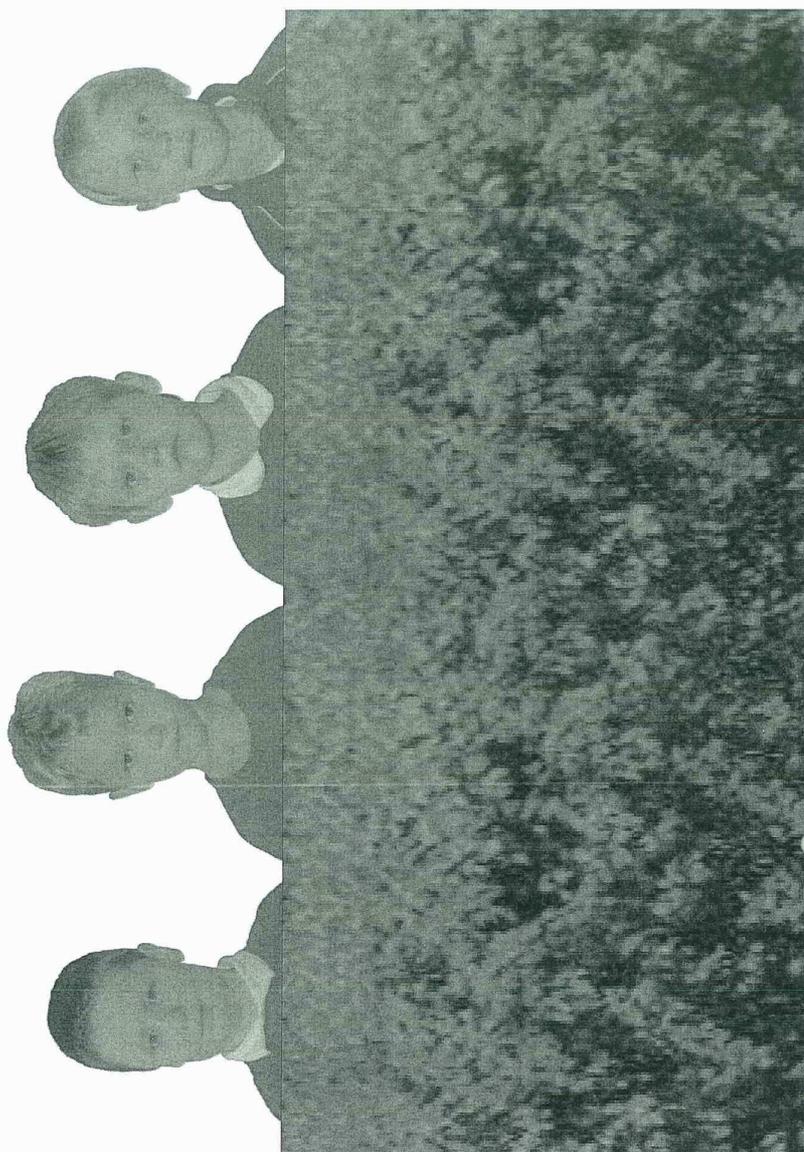
Parent's (or guardian's) signature _____

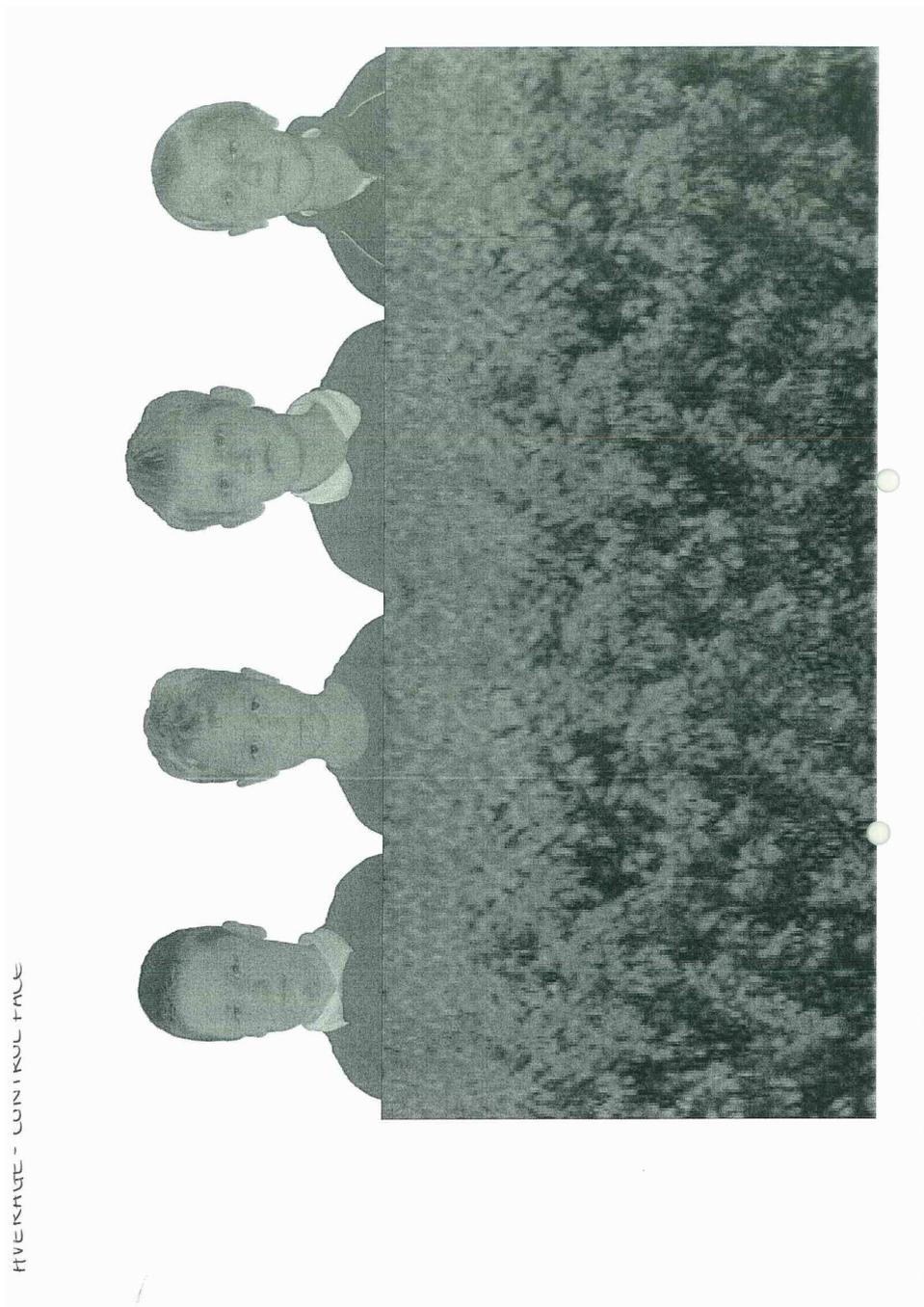
Date _____

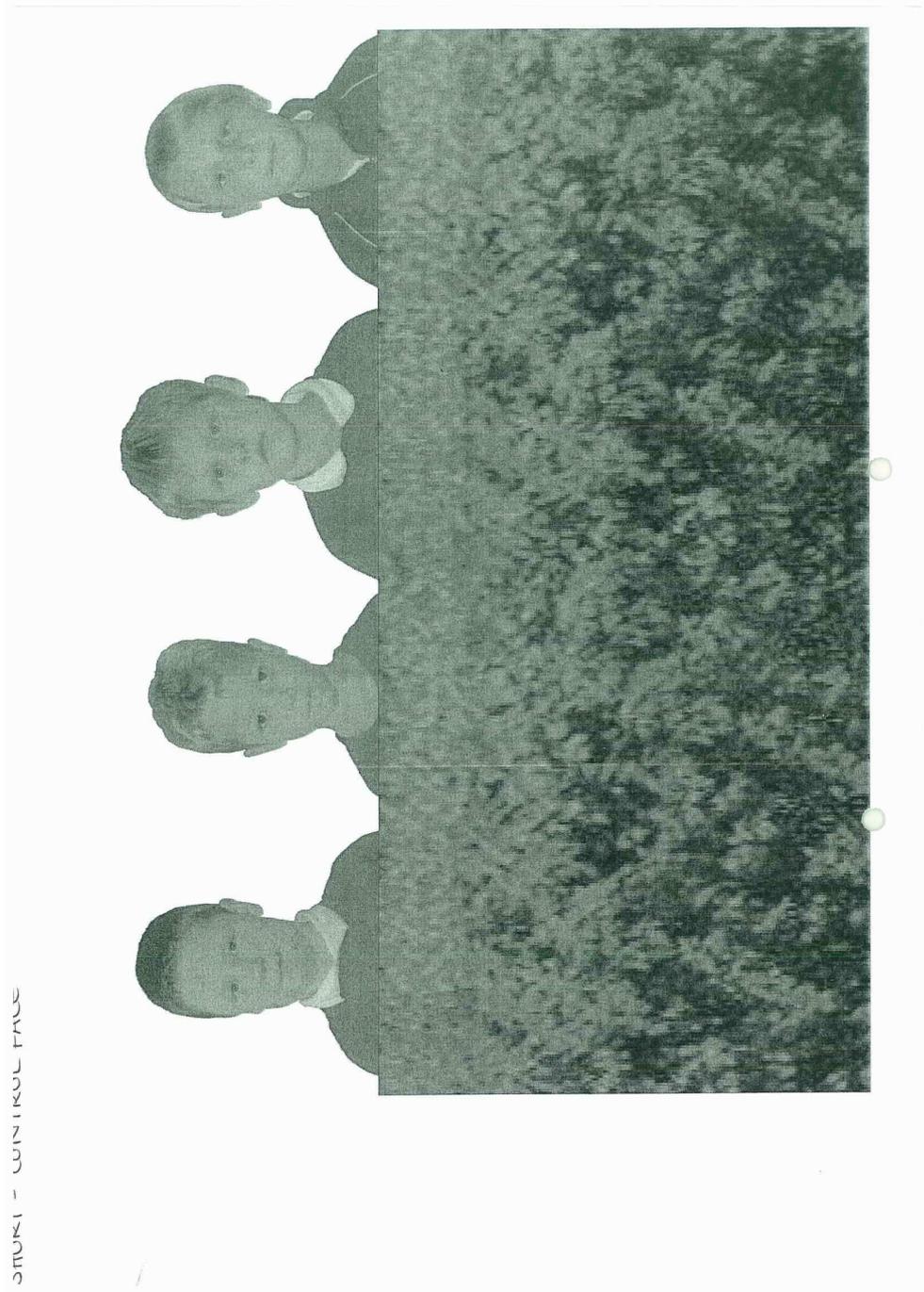
APPENDIX T

Picture stimuli for Study 6

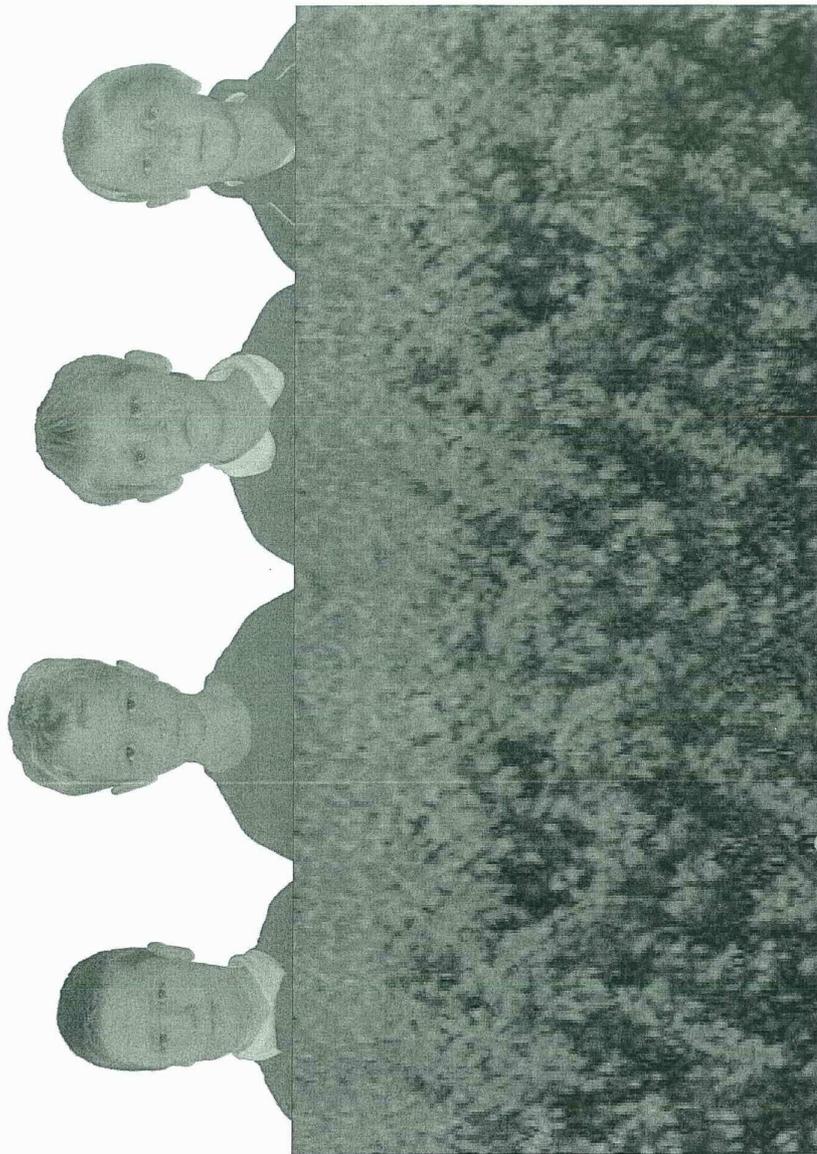
TALL - CONTROL FACE

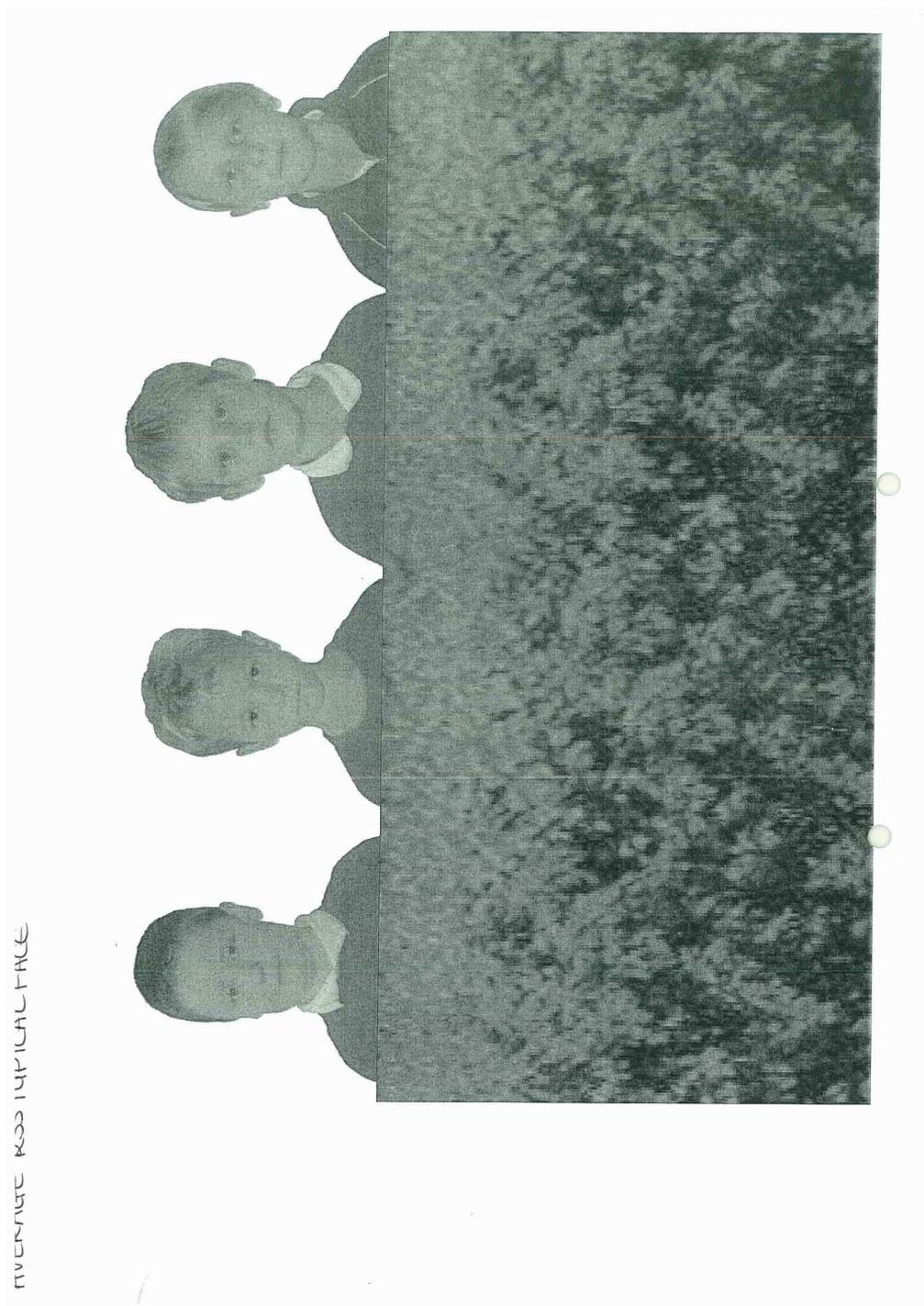




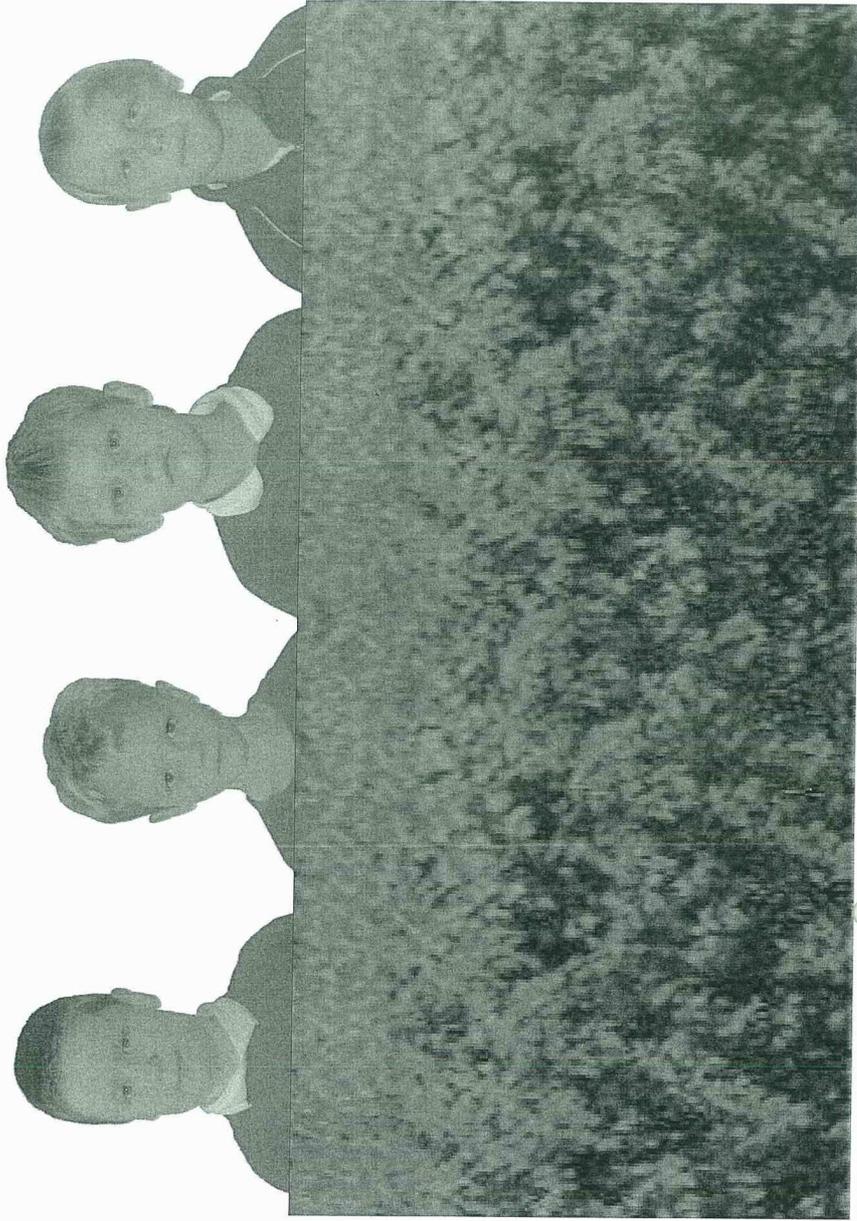


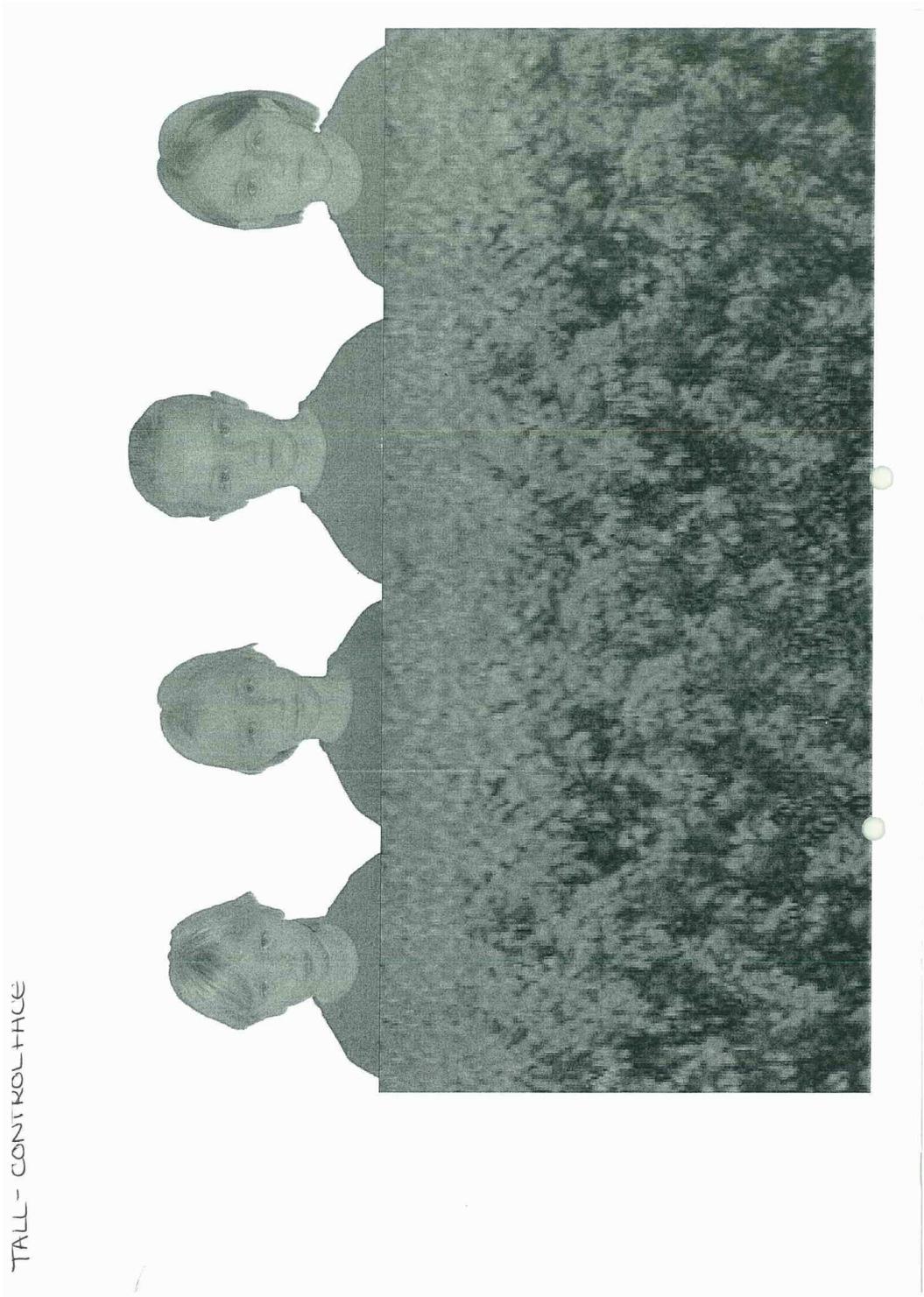
144 - KDS TYPICAL FACE



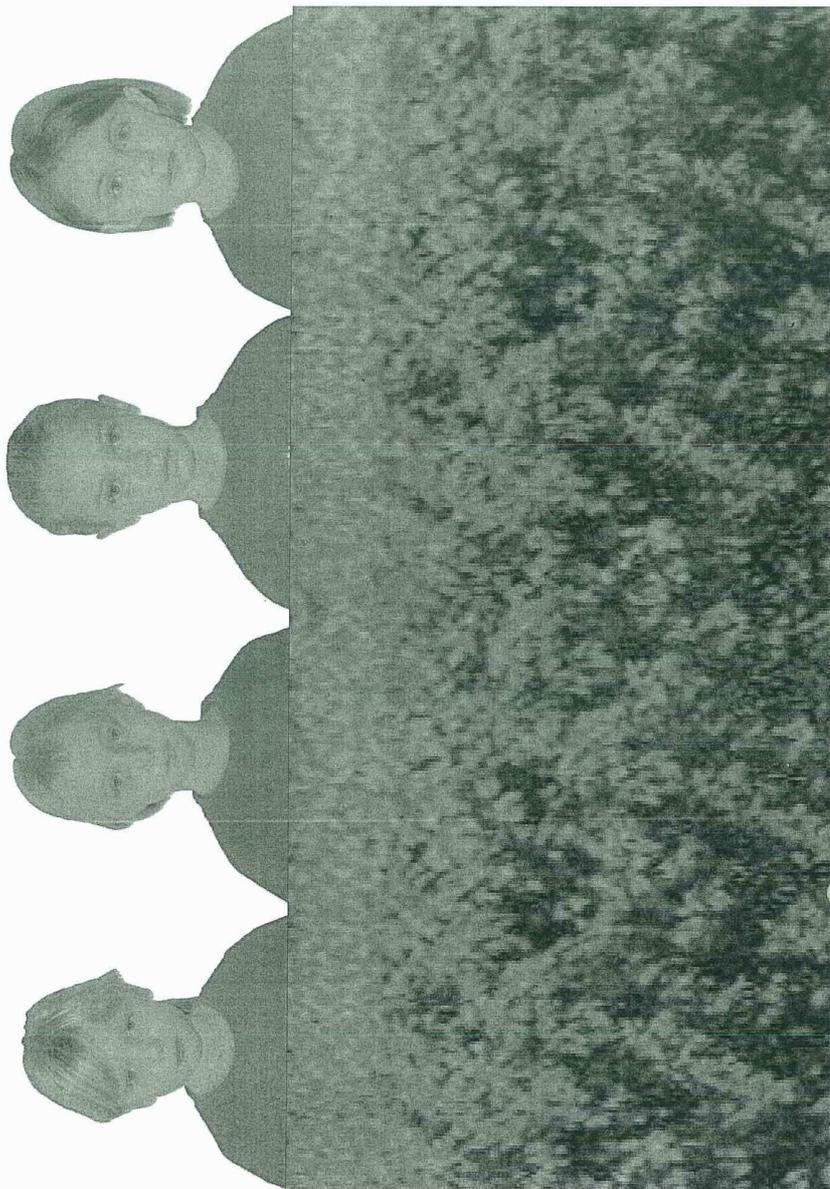


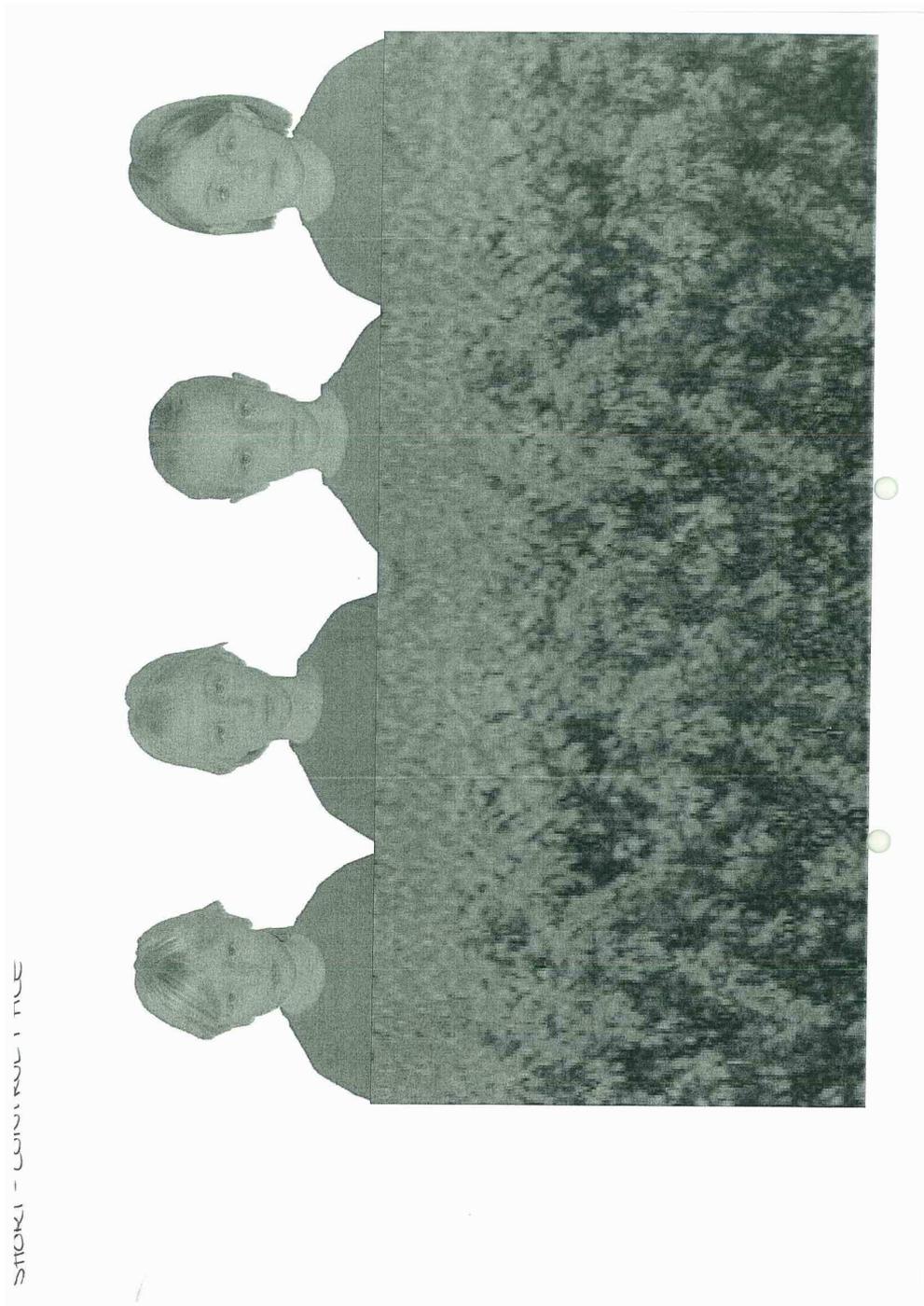
STUKI - R03 14MICAL FALB

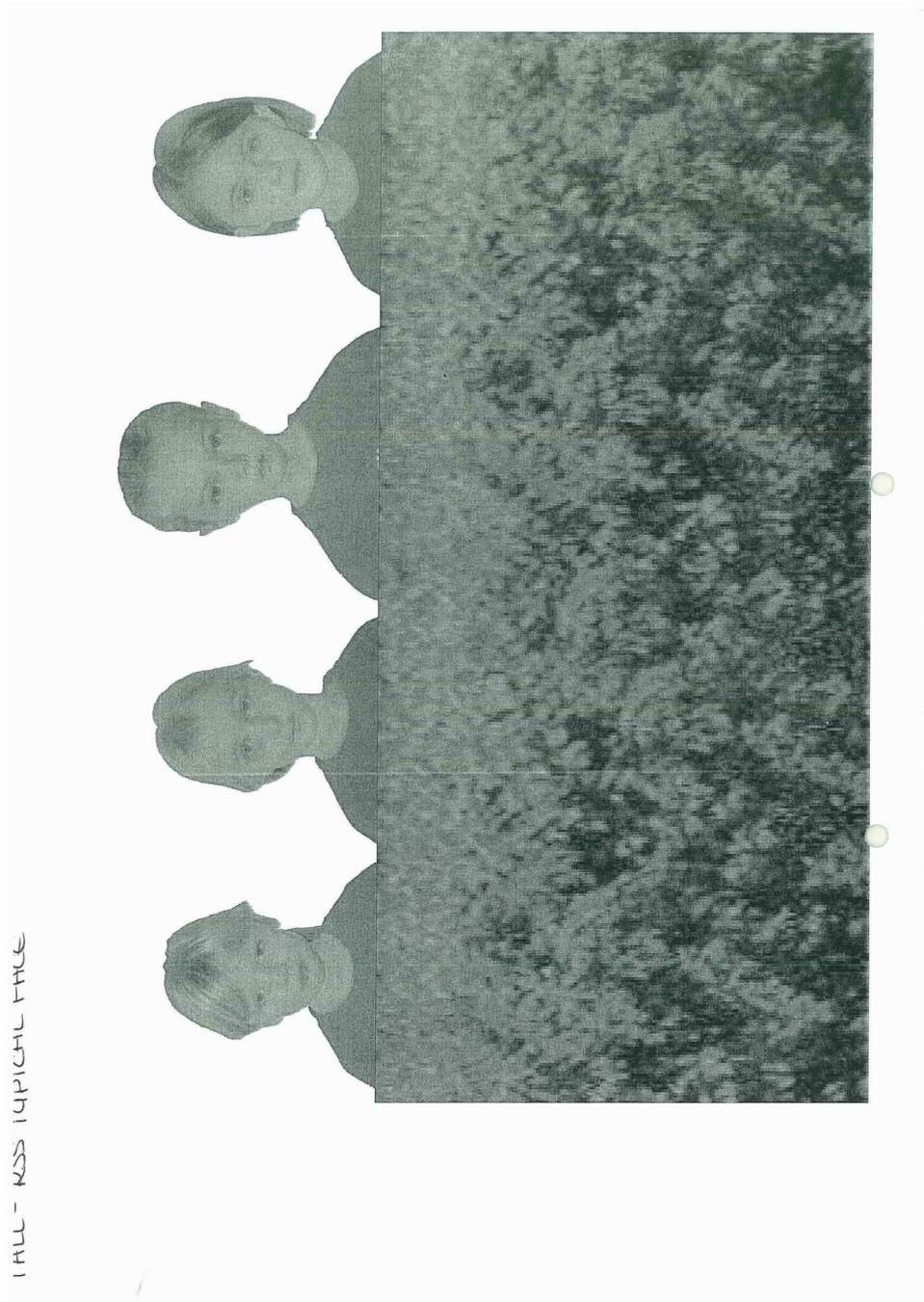




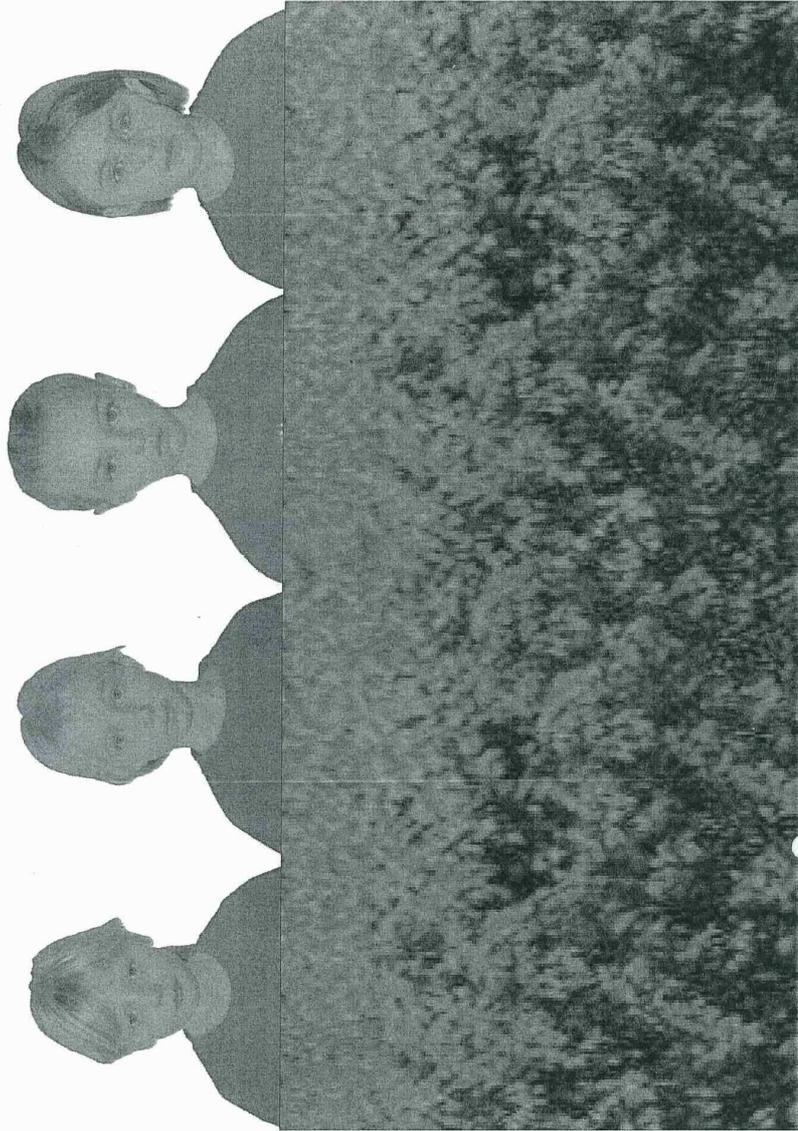
AVERAGE - CONTROL FACE



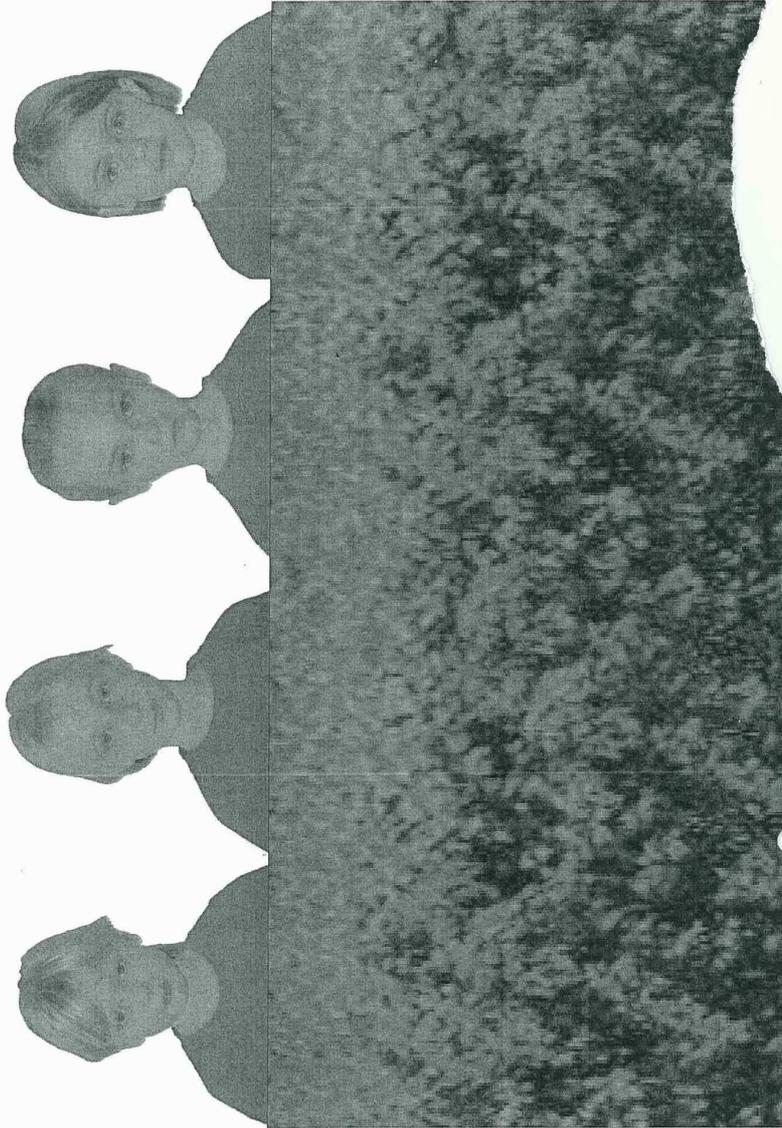




AVERAGE - RSS TYPICAL FACE



SHORT - RSS TYPICAL FACE



APPENDIX U

Adult response sheet for study 6

Personal Information

Age _____

Gender (please circle) Male Female

Instructions

Please look at the photograph of the 4 boys overleaf, look specifically at the boy with the star above his head and rate him on the scales on the opposite page.

Repeat for the picture of the 4 girls, again looking at the girl with the star above her head and rating her on the scales.

Picture code _____

Please indicate by circling the appropriate number on the scales, where you think the person in the photograph will fall.

Good looking				Not Good Looking		
1	2	3	4	5	6	7

Baby – Faced				Mature – Faced		
1	2	3	4	5	6	7

Friendly				Unfriendly		
1	2	3	4	5	6	7

Physically Strong				Physically Weak		
1	2	3	4	5	6	7

Bossy				Not Bossy		
1	2	3	4	5	6	7

Intelligent				Unintelligent		
1	2	3	4	5	6	7

Mature				Immature		
1	2	3	4	5	6	7

Independent				Dependent		
1	2	3	4	5	6	7

Cute				Not Cute		
1	2	3	4	5	6	7

Caring				Uncaring		
1	2	3	4	5	6	7

How old do you think the child in the picture is? _____

APPENDIX V

Child response sheet for study 7

Participant sex and age								
Picture Number								
Good Looking								
Baby Faced								
Friendly								
Physically Strong								
Bossy								
Intelligent								
Grown Up								
Needs Looking After								
Cute								
Caring								
Would like to play with								
Age								