Archives of Disease in Childhood 1994; **71**: 490–496

ORIGINAL ARTICLES

Cognitive abilities associated with the Silver-Russell syndrome

Kelly Y C Lai, David Skuse, Richard Stanhope, Peter Hindmarsh

Abstract

There is no consensus opinion on whether or not cognitive impairments are found in the Silver-Russell syndrome. An investigation of a substantial sample was undertaken, using standardised assessments, in 20 boys and five girls aged 6·0 years to 11·8 years. Mean (SD) birth weights were −2·65 (0·95) SD scores, corrected for gestation. At evaluation the children had a mean (SD) age of 8·8 (1·8) years and a mean height of −2·26 (1·5) SD scores. Tests of cognitive abilities included assessments of general intelligence, reading and arithmetic attainments, and a cognitive processing task. Most had some degree of developmental delay: mean (SD) full scale IQ was 86 (24); 32% scored within the learning disability range (that is, IQ <70); 40% were reading at least 24 months below their chronological age. Current head circumference correlated highly with full scale IQ. Assessments of special educational needs had been completed on 36%; 48% were receiving speech therapy. Approximately half of children with the Silver-Russell syndrome have significant impairment of their cognitive abilities.

(*Arch Dis Child* 1994; **71**: 490–496)

Child and Adolescent Psychiatry Unit, Department of Psychiatry, Prince of Wales Hospital, Shatin, Hong Kong
K Y C Lai

Institute of Child Health, London, Behavioural Sciences Unit
D Skuse

Medical Unit
R Stanhope

Cobbold Laboratories, Middlesex Hospital, London
P Hindmarsh

Correspondence to:
Professor Skuse.

Accepted 22 August 1994

In 1953, Silver described two children with body asymmetry, short stature, low birth weight, and abnormal sexual development.[1] A year later, Russell reported five children who presented similarly with low birth weight and short stature, but only two had asymmetry.[2] In addition, he noted the presence of characteristic craniofacial features and a shortened incurved fifth finger. In Silver's subsequent review of 29 similar cases reported in the literature, he found that these and other clinical features were often associated, but none was invariably present in any one case.[3] Features that were more often reported included low birth weight (93%), short stature (93%), asymmetry (78%), clinodactyly (76%), and a craniofacial appearance similar to that described by Russell (50–62%).[2]

The current view is that the Silver-Russell syndrome is a single entity,[4] although no consistent criteria have been established for its diagnosis. Low birth weight and short stature are almost always present. Tanner *et al* have argued that it is probably a distinct condition from non-specific intrauterine growth retardation.[5] It is characterised in particular by the presence of distinctive craniofacial features (small triangularly shaped face with relatively large forehead and small chin, downturned corner of the mouth sometimes known as a 'shark's mouth' appearance, and low set ears). Limb asymmetry, clinodactyly, and excessive sweating lend support to the diagnosis. There is no catch-up postnatal growth, so that affected children remain short and very lean through to middle childhood. Growth hormone deficiency may coexist. There are no sex or race differences in prevalence. The aetiology of the intrauterine growth impairment and the dysmorphic features is unknown.

While the physical development of affected children has been studied in detail,[5–7] their cognitive development has received much less attention. Reports in the literature are inconsistent, and most are based upon clinical impressions. There do not appear to be any published reports of cognitive abilities based on formal measurements. Silver concluded in his review of 29 cases that 'significant mental retardation' occurred more often than would be expected by chance.[3] In the series of Tanner *et al*, the intellectual abilities of 11 children were found to be within the normal range.[5] In a sample of 15 children described by Saal *et al*, six of them were found to have either specific developmental delays (especially in the area of language) or frank mental retardation.[6] Yet Patton has expressed the opinion that 'normal IQ is the rule'.[4] Impairment of motor development has also been reported, and is usually attributed to an age inappropriate lack of muscle bulk and power.

We hypothesised that, similar to reported samples of low birthweight children, the cognitive abilities of children with Silver-Russell syndrome were likely to be impaired. Were this to be the case parents could be advised about the possibility of learning difficulties, and hence the potential need for extra educational provisions.

Subjects and methods

The Child Growth Foundation (a charitable organisation for families with children with growth problems) and the growth clinics of

two university teaching hospitals were approached for the names of children who had been diagnosed as having the Silver-Russell syndrome. A total of 30 families were contacted of whom 25 agreed to take part. Eighteen were recruited from the former source and seven from the latter. Those who did not agree did not differ from the remainder in terms of demographic indices, on the basis of available information. The inclusion criteria for the recruitment of subjects were as follows. Firstly, the diagnosis of Silver-Russell syndrome was made when three out of the following five diagnostic features were present: (i) low birth weight (at least 2 SDs below the population mean, adjusting for maternal stature, gestation, ordinal position of the child (first or other born), and gender according to the method of Tanner and Thomson[8]); (ii) short stature at the time of the original diagnosis (height for age at least 2 SDs below the population mean[9]); (iii) a characteristic craniofacial appearance as described by Russell[2]; (iv) limb or body or facial asymmetry; and (v) clinodactyly. Secondly, the age range was restricted to those between their sixth and 12th birthdays, in order to achieve sufficient homogeneity to allow the assessment of all subjects with the same instruments.

CLINICAL AND GROWTH DATA

Relevant clinical information about the children was obtained from their hospital case notes and, where appropriate, supplemented by parental accounts. This included: (i) diagnostic features, which were additionally ascertained by clinical examination of the children; (ii) weight and height at the time of diagnosis; (iii) the presence of other clinical features, including a history of major feeding problems in infancy and early childhood, hypoglycaemic episodes, and excessive sweatiness; and (iv) coexisting significant medical illnesses. In addition, the children's general practitioners were approached to provide information on the pregnancy, birth, and the children's anthropometric data at birth (weight, length, and head circumference).

The children's current weight and height were measured at the time of assessment using, respectively, a SECA electronic weighing scale (model 770; Vogel and Halke GmbH) and a Raven Magnimetre stadiometer (Raven Equipment; Castlemead Publications). Their occipitofrontal head circumference was measured using a tape made of non-stretchable material according to the method described by Cameron.[10]

Because anthropometric measurements were obtained at different ages for each child, the data have been standardised for age and gender, and are expressed in SD scores. Computation of the SD scores was undertaken by the Centers for Disease Control anthropometric analysis system.[11] Weight for height ratios were similarly calculated. Occipitofrontal circumferences were also standardised for age and gender[12] and are expressed as SD scores.

MEASUREMENT OF COGNITIVE ABILITIES

The following instruments were administered: (1) the Wechsler intelligence scale for children (WISC), 3rd edition UK.[13] Eight out of 13 possible subtests were administered. Pilot studies had shown that child cooperation for the full assessment was compromised by the full version. The choice of subtests was determined by the factorial structure of the instrument (p 79) and the guidelines for prorating scores (p 54).[13] (2) The Neale analysis of reading ability, revised British edition.[14] The child is asked to read short stories of increasing difficulty until 16 or more errors are made in passages 1–5, or 20 errors in passage 6. A set of comprehension questions is provided after each passage to assess the child's understanding of the story. Separate reading ages can be computed for rate, accuracy, and comprehension. (3) The matching familiar figures test (MFF20).[15] This aims to assess an aspect of cognitive processing which is believed to be closely linked to the child's ability to attend to task, on a dimension ranging from reflectivity to impulsivity. It involves asking the child to match a sample picture, choosing from six simultaneously presented options. The time between the presentation of the pictures and the child's first response is recorded (the 'reaction' time). If the child fails to supply the correct response the first time, s/he is asked to continue until the correct answer is given. The total number of erroneous responses is also recorded.

STATISTICAL ANALYSIS

Most measurements were made on ordinal or interval scales. Summary statistics are presented, where appropriate, as mean values and 1 SD. Comparison of means and correlations employed standard parametric methods of analysis where scale properties permitted. Where the data for the sample were compared with a hypothetical population mean (for example, for IQ) a one sample t test was used with $n-1$ degrees of freedom.

Results

DEMOGRAPHIC FACTORS

The sample consisted of 20 boys and five girls. Their mean (SD) age was 8·75 (1·7) years. All were white except one (case 11) who was of West Indian parentage. Twenty two (88%) of the children were living with both biological parents. The remaining three were living with, respectively, a widowed mother (case 5), adoptive parents (case 11), mother and stepfather (case 14). Assessment of social class, based on father's occupation[16] gave the following distribution: eight (32%) were in managerial or professional occupations, three (12%) in assistant professional/clerical occupations, nine (36%) in craft/personal/sales related occupations, two (8%) worked as plant operatives, and two (8%) were unemployed. Eighteen (72%) of the families had purchased their own properties, seven (28%) were in rented municipal housing.

Table 1 Anthropometric measurements

Case No	Sex	At birth			At diagnosis				Growth hormone treatment	Current				
		Weight (SD)	Length (SD)	OFC* (SD)	Age (years)	Weight (SD)	Height (SD)	Wt/ht† (SD)		Age (years)	Weight (SD)	Height (SD)	Wt/ht† (SD)	OFC* (SD)
1	M	−0·63	−1·43	N/A	2·5	−2·54	−2·91	−1·02	−	7·8	−2·06	−2·71	−0·34	0·20
2	M	−3·28	−0·19	−1·00	3·5	−2·08	−1·90	−1·34	+	10·2	−1·2	−0·62	−1·22	−1·3
3	M	−3·25	N/A	N/A	2·8	−3·22	−2·45	−2·44	+	9·0	−1·57	−1·05	−1·31	N/A
4	M	−2·84	N/A	1·25	2·9	−3·72	−3·38	−2·59	+	7·3	−2·32	−1·83	−1·63	1·00
5	M	−3·66	−4·89	N/A	2·5	−4·45	−9·59	N/A	+	8·4	−4·29	−7·32	−0·92	N/A
6	M	−2·80	−9·78	N/A	4·0	N/A	N/A	N/A	+	7·5	−2·23	−1·95	−1·39	−2·20
7	M	−3·03	−3·95	−1·88	2·0	−3·30	−2·75	−2·83	+	7·6	−1·44	−0·52	−1·57	0·10
8	M	−3·22	N/A	N/A	9·2	−2·29	−2·42	−1·23	−	9·8	−2·12	−2·41	−0·90	−2·90
9	F	−3·15	N/A	N/A	3·2	−4·25	−4·76	−2·28	+	11·8	−1·79	−1·44	N/A	−2·54
10	M	−1·77	−1·41	−0·85	7·6	−3·18	−4·08	−1·11	+	9·7	−2·09	−2·76	−0·40	−0·3
11	M	−2·19	−3·95	−0·34	4·5	−2·08	−2·04	−1·21	−	6·6	−2·62	−2·30	−1·69	N/A
12	F	−4·10	−9·17	−3·85	0·7	−4·96	−5·31	−1·44	−	7·6	−4·13	−4·42	−3·36	−5·70
13	M	−1·58	N/A	N/A	1·6	−3·63	−2·99	−2·94	+	8·8	−2·36	−2·65	−1·05	−0·35
14	M	−3·03	−3·01	−2·73	1·9	−3·75	−3·04	−3·30	−	9·0	−2·94	−2·41	−2·58	−2·10
15	M	−0·88	−0·63	N/A	4·0	−3·68	−3·93	−2·44	+	10·0	−1·32	−0·76	−1·26	−1·80
16	F	−3·94	N/A	N/A	2·7	−4·13	−2·98	−3·09	−	6·0	−2·75	−2·31	−2·05	−1·35
17	M	−3·88	N/A	−4·27	6·4	−3·21	−3·13	−1·97	+	9·0	−1·50	−0·89	−0·67	−3·95
18	M	−3·47	−4·11	N/A	3·0	N/A	−3·46	N/A	+	9·1	0·07	−0·06	−1·39	−3·00
19	M	−2·40	0·85	−0·85	3·5	−2·19	−2·71	−0·89	+	11·6	−1·15	−1·25	N/A	0·80
20	F	−3·08	−1·65	−2·56	5·2	−3·43	−3·21	−2·37	+	10·3	−1·99	−2·32	N/A	−2·15
21	M	−1·33	−0·63	1·20	4·5	−2·13	−2·83	−0·66	−	6·3	−1·85	−3·04	0·21	0·25
22	M	−1·85	−2·70	0·00	0·8	−2·86	−2·91	−0·67	−	6·6	−2·90	−3·27	−1·54	−1·60
23	F	−1·64	N/A	N/A	8·5	−2·28	−2·41	−1·11	−	9·6	−2·24	−2·33	−1·29	0·90
24	M	−2·94	−3·86	−0·85	1·3	−4·15	−4·54	−1·67	−	7·5	−2·97	−3·00	−1·68	−0·60
25	M	−2·32	N/A	N/A	5·7	−3·28	−3·68	−1·72	+	11·8	−0·84	−1·00	N/A	0·63

*OFC=occipitofrontal circumference; †wt/ht=weight for height ratio. N/A=data not available.

CLINICAL DATA

The clinical features of the sample are presented in tables 1 and 2. The mean (SD) age at diagnosis was 3·72 (2·32) years. Fifteen children (60%) were subsequently started on growth hormone treatment. Their mean duration of treatment at the time of the assessment of their cognitive abilities was 3·6 (1·7) years.

AUXOLOGY

The mean (SD) birth weight of the sample was 2000 (610) g and the mean standardised[8] birth weight score was −2·65 (0·95) SD scores. Eighteen (72%) of the children had a birth weight more than −2 SD scores. Five (20%) were between −1 and −2 SD scores, and the remaining two (8%) were between 0 and −1 SD scores. Seventeen (68%) were born between 38 and 42 weeks' gestation, five (20%) between 36 and 38 weeks, and three (12%) at below 36 weeks. Three (12%) of the children were one of twins (cases 9, 17, 18). The pregnancy and neonatal period were uncomplicated in 21 of the cases. The remaining four had either mild asphyxia (case 19), hypothermia (cases 12 and 16), or neonatal sepsis (case 9).

The mean (SD) standardised height of the sample at the time of their initial diagnosis (n=24) was −3·45 (1·53) SD scores, of whom 23 (92%) were more than 2 SD scores below the 50th centile; the mean age of the children at this time was 3·74 (2·3) years. The mean (SD) standardised weight at diagnosis (n=23) was −3·24 (0·83) SD scores and the corresponding figure for weight for height was −1·83 (1·2) SD scores. At the time of their cognitive testing the mean (SD) age of the sample was 8·8 (1·8) years, their mean height was −2·19 (1·48) SD scores, their mean weight was −2·1 (0·95) SD scores, and their mean weight for height (n=21) was −1·33 (0·77) SD scores.

Table 2 Clinical features and IQ scores

Case No	Craniofacial features	Asymmetry	Clinodactyly	Feeding problems	Hypoglycaemia episodes	Full scale IQ	Verbal IQ	Performance IQ
1	+	+	−	+	N/K	102	91	115
2	+	+	+	+	−	105	111	96
3	+	+	+	+	−	96	95	99
4	+	+	+	−	+	126	119	127
5	+	+	+	+	N/K	68	92	50
6	+	−	+	+	−	94	92	96
7	+	+	+	+	+	107	111	101
8	+	−	+	−	−	57	65	55
9	+	+	+	+	−	85	83	91
10	+	−	+	+	−	62	58	71
11	−	+	+	+	+	103	100	107
12	+	−	−	+	−	61	59	69
13	+	−	+	+	−	58	66	55
14	+	−	+	−	+	72	74	76
15	+	+	+	+	−	71	81	68
16	+	+	+	+	+	81	89	77
17	+	+	+	+	N/K	81	107	60
18	+	+	+	+	−	63	63	68
19	+	+	+	+	+	126	122	123
20	−	+	+	+	−	46	52	47
21	+	+	+	+	+	77	87	71
22	+	+	+	+	+	68	70	71
23	+	+	+	+	−	106	100	113
24	+	+	+	−	+	130	141	104
25	+	+	+	−	−	102	104	97

All the fathers and 22 (88%) of the mothers were of average height (between the 3rd and 97th centile).[9] The remaining three mothers were either at or below the 3rd population centile. There was a considerable range in the children's head circumferences, which were on average in the lower range of population norms; mean (SD) −1·27 (1·73) SD scores.

CHARACTERISTIC FEATURES

Twenty three (92%) of the children had the distinctive facies, with a small triangularly shaped face, relatively large forehead, a small chin, downturned corners of the mouth, and low set ears. Body asymmetry was present in 19 (76%) and incurving of the fifth finger was found in 23 (92%) of the sample.

HISTORY OF MAJOR FEEDING PROBLEMS AND HYPOGLYCAEMIC EPISODES

Major feeding problems leading to poor weight gain in infancy and early childhood were reported in 20 (80%) of the cases. Physical causes for the feeding problems were not found in any of the cases. Hypoglycaemic episodes after a short period of fasting were documented in four (16%) of the children. In another five (20%), episodes resembling hypoglycaemia that manifested as drowsiness, lethargy, excessive sweatiness, or irritability, which were reversed by giving them food, were reported by the parents, but had not been medically investigated. Such episodes were thought to be more common during early childhood, but all were reported to have persisted until the present investigation.

CONCURRENT MEDICAL DIAGNOSIS

The results of investigations of growth hormone status was available for 18 of the children, four of whom were found to have concomitant growth hormone deficiency. Of these four children, one also had cutaneous neurofibromatosis (case 13), one had congenital heart disease and one had an α_1-antitrypsin deficiency (case 17). The children who were subsequently treated with growth hormone (n=15) and those who were not (n=10) were similar in age when their diagnosis was made, and had similar standardised weight, height, and weight for height SD scores at that time. When seen in the course of this investigation those who were receiving growth hormone were significantly older (mean (SD) 9·47 (1·5) years) than the remainder (mean 7·67 (1·4) years; t=3·1, df 23, p=0·006). They were not, however, significantly taller: mean (SD) −1·84 (1·8) and −2·82 (0·7) SD scores respectively, and their weights for height were similar: treated group mean −1·16 (0·4) and untreated group −1·52 (1·0).

Table 3 Results of WISC intelligence test

Test	*Silver-Russell syndrome*				
	Mean (SD)	*95% Confidence intervals*	*Mean (SD) population*	t	*p Value*
Full scale IQ	85·9 (23·7)	76·6 to 95·2	100 (15)	3·0	<0·01
Verbal IQ	89·3 (22·6)	80·4 to 98·2	100 (15)	2·4	<0·05
Performance IQ	84·3 (23·5)	75·1 to 93·5	100 (15)	3·3	<0·01
Verbal subtests					
Comprehension	8·7 (4·1)	7·1 to 10·3	10 (3)	1·6	NS
Information	8·5 (4·0)	6·9 to 10·1	10 (3)	1·8	NS
Similarities	7·6 (4·5)	5·8 to 9·4	10 (3)	2·7	<0·01
Vocabulary	7·8 (4·1)	6·2 to 9·4	10 (3)	2·7	<0·01
Performance subtests					
Block design	8·2 (5·0)	6·1 to 10·1	10 (3)	1·8	NS
Object assembly	6·9 (3·8)	5·4 to 8·4	10 (3)	4·0	<0·001
Picture arrangement	7·6 (4·0)	6·0 to 9·2	10 (3)	2·9	<0·01
Picture completion	7·2 (3·6)	5·8 to 8·7	10 (3)	3·8	<0·001
Other subtests					
Arithmetic	7·7 (3·9)	6·1 to 9·3	10 (3)	2·9	<0·01

INTELLECTUAL ABILITY

A wide range of abilities was found (table 3). The mean (SD) full scale IQ (85·9 (23·7)) of the sample was, however, nearly 1 SD below that of the general population (mean 100 (15)). Nine (36%) of the children scored within the average range of abilities (full scale IQ 85–115) and three (12%) had above average abilities (IQ 116–130). In contrast, five (20%) had scores in the borderline range of mental retardation (IQ 70–84) and eight (32%) were in the range associated with mild/moderate learning disability (IQ <70). The three children with the highest scores were distinguished by having normal head circumferences at birth (mean −0·15 SD scores) and at follow up (mean 0·4 SD scores). The scores of the group as a whole on all eight verbal and non-verbal performance subtests of the WISC were for the most part significantly below the population mean (table 3). The children did relatively better on verbal skills.

The small number of girls in the sample limited the confidence of findings comparing the performance of boys and girls on cognitive testing. However, girls (n=5) did have lower full scale IQs (mean (SD) 68·2 (15·7)) than boys (n=20) (mean 90·3 (23·5)). This difference did not quite reach statistical significance (p=0·06), nor did that for the difference in mean (SD) performance IQ (girls 71 (15·9); boys 87·6 (SD 24)). Girls did have significantly lower verbal IQ scores (mean 70·6 (15·6)) than boys (mean 94·0 (21·8); t=2·2; df 23, p=0·03). When the various anthropometric measurements were correlated with IQ scores using Pearson's correlation test, *current* head circumference measured in standardised scores was found to be significantly correlated with full scale IQ (r=0·6, p=0·004), performance IQ (r=0·62, p=0·002), and verbal IQ (r=0·49, p=0·02). Correlations between standardised head circumference *at birth, and between growth of head circumference from birth,* and the current IQ scores failed to reach statistical significance. In both cases examination of the scatter plot of those variables and IQ suggested there probably was a relationship, but there were insufficient data (52% of sample) to be confident about it.

READING AND ARITHMETIC

On average the children's reading competence was well below their chronological age (table 4). Their mean (SD) reading comprehension was 15·4 (23·8) months delayed, their

Table 4 Arithmetic and reading assessments, with indication of significant degrees of reading retardation

Case No	Age (months)	Arithmetic scaled score (maximum 19)	Reading accuracy age (months)	Reading comprehension age (months)	Reading rate age (months)
1	94	9	67*	63*	63*
2	122	14	157	136	109
3	108	9	128	110	90
4	88	11	94	98	113
5	101	6	98	95	153
6	90	13	69	81	74
7	91	11	93	95	130
8	118	6	59*	61*	59*
9	142	6	94*	98*	107*
10	116	2	75*	76*	76*
11	80	10	68	66	77
12	91	5	59*	59*	59*
13	104	1	70*	73*	73*
14	108	7	83*	86	87*
15	120	9	92*	81*	87*
16	72	4	59	59	59
17	108	11	87	98	87
18	109	1	87	89	107
19	139	9	152	157	147
20	124	1	59*	59*	59*
21	76	7	69	76	65
22	78	6	78	68	81
23	115	12	106	110	83*
24	90	13	157*	126*	121*
25	142	10	106*	119	113*

*Indicates a value ≥24 months behind chronological age.

accuracy was lower by a mean of 14·4 (29·1) months, and their rate of reading by a mean of 13·8 (28·9) months. We did not have an appropriate regression equation that would allow us to compute values for 'specific reading retardation', allowing for the children's IQs. However, the proportion falling more than 24 months behind their chronological age in respect of reading accuracy or comprehension is shown in table 4. The wide SDs indicate the fact that a minority were reading competently: 24% had a higher level of comprehension, 20% a greater reading accuracy, and 24% a reading rate above that expected for their chronological age. Arithmetic competence was not so severely affected, with a mean delay in relation to chronological age of 7 (24) months, and 32% of children performing at or above the expected level. Those children with above average reading and arithmetic abilities across the four areas of attainment also had above average IQs, a mean difference from the remainder of the sample of 21 points higher.

COGNITIVE PROCESSING

When tested with the matching familiar figures task the mean (SD) reaction time scores were 11·0 (4·12) for boys and 8·69 (3·25) seconds for girls. Two boys and one girl were excluded from the analysis on account of extreme values. The mean (SD) error score was 24·95 (11·71) for boys and 33·60 (16·80) for girls. The differences in mean reaction time and error scores between the boys and the girls in our sample were not statistically significant. These results are very similar to those obtained from a sample of 7–8 year old normal controls in a study by Taylor *et al* (E Taylor, personal communication) where the mean (SD) reaction time for boys (n=42) was 13 (8·7) seconds, and for girls (n=48) was 11·9 (9·2) seconds. The corresponding mean error scores were 30 (12) and 30·1 (13) respectively.

EDUCATION

Nine (36%) of the children had been formally statemented as having special educational needs: two of them had been transferred to special schools, the other seven were receiving remedial help in mainstream schools. Their main areas of difficulty tended to be in the area of reading and language skills. Another three children were being given remedial help without having been formally statemented. Twelve children (48%) had received speech therapy because of articulation or other developmental speech problems.

Discussion

The results of our study reveal that children with the Silver-Russell syndrome have cognitive abilities that are, on average, 1 SD below the general population mean in terms of both verbal and non-verbal skills. One third of them have scores within the learning disability range. Underachievement in reading and arithmetic was present in the majority of children. It was not possible with such a small sample to undertake analyses that would make allowance for the children's overall IQ but it is notable that those children with above expected performance in relation to their age were also children with significantly higher IQs than the remainder. Nearly half of the group required remedial education, and a similar proportion had received speech therapy. In a test of cognitive processing, these children did not appear to have poorer attention, in terms of impulsivity/reflectiveness, than a normal age equivalent sample drawn from the general population. Although we did not have direct measures of their parents' intellectual functioning, it is notable that the majority of parents were from the upper end of the social class spectrum, and the ascertainment bias of the sample would, if anything, be expected to have identified children with above average abilities.

Knowledge of the cognitive functioning of children with the Silver-Russell syndrome is of both theoretical and clinical significance. Measures of the global intelligence of children with low birth weight are usually reported to be 0·5–1 SD below those of normal controls.[17–19] Specific cognitive deficits may also be present, including poor perceptual motor skills,[20] expressive and receptive language problems,[21–24] and features suggestive of attention deficit disorder (such as distractibility, inattention, and high levels of activity).[25 26] However, most reports do not distinguish between those whose birth weights were consonant for their gestational age and those who were light for dates.[27] It is thought that when intrauterine growth retardation commences relatively early in pregnancy, resulting in a reduction in both birth weight and length ('symmetrical' intrauterine growth retardation), in utero brain development is more likely to be affected than when the onset is relatively late ('asymmetrical' intrauterine growth retardation).[28] Lower scores on various measures of mental development have been found in the

'symmetrical' intrauterine growth retardation group than the 'asymmetrical' group.[29–31] The intrauterine growth retardation of the Silver-Russell syndrome is believed to begin early in pregnancy.[2 5 32] Other factors that have been shown to play a part in modifying the cognitive development of children with low birth weight include the sex of the child and socioeconomic factors, which may overshadow perinatal complications such as asphyxiation, neonatal hypoglycaemia, and prematurity.[26 28 33–36] Boys, and children from lower socioeconomic classes are more at risk. The finding that girls in this sample had poorer cognitive abilities than boys is contrary to expectation.

The short stature of children with the Silver-Russell syndrome is unlikely to make any significant independent contribution to the presence of cognitive impairments, if any.[37] Where short stature syndromes are associated with specific cognitive deficits, as in some cases of hypopituitarism,[38] or the Turner's syndrome,[39 40] this is usually due to the underlying pathology rather than the growth disorder itself. On the other hand, studies have found that in general individuals who are relatively small in size for their age may be perceived by others to be younger than they really are.[41 42] Accordingly, children who are short may elicit a pattern of care from adults that hampers their emotional and psychological development, and this may in turn affect other aspects of their functioning.[37]

These findings suggest that the general cognitive abilities of children with the Silver-Russell syndrome are at the lower end of the range reported for representative samples of low birthweight children.[21 43 44] However, low birth weight is a heterogenous condition, and their performance may be similar to other children whose intrauterine growth retardation commences early in pregnancy.[29–31] Other factors known to influence the cognitive development of children with intrauterine growth retardation probably played less significant a part in our study sample. Complications during pregnancy and birth were seldom reported and most came from relatively advantaged socioeconomic backgrounds. However, many of the children had persistent hypoglycaemia, and this may well have been an aetiological factor for impaired neuronal development. Given their social backgrounds the children's relatively poor performance was, therefore, all the more significant; it would have been interesting to compare it with that of their siblings but we were unable to undertake those assessments. There was no indication that parents who agreed to take part in the study, or the paediatricians whose cases were recruited, agreed to cooperate with the research because of concern about the children's psychosocial or intellectual development.

The finding of a correlation between the children's IQ scores and current (as well as possibly birth) occipitofrontal circumference echoes similar observations from other studies of children with intrauterine growth retardation.[34 35 45] Children with a small head circumference at birth due to intrauterine growth retardation tend to continue to have smaller than average heads in later childhood and adolescence.[18 31 34 35] Any catch-up head growth that occurs should have done so within the first postnatal year or two,[31 46] so measuring and monitoring these children's head circumference from birth might allow the early identification of those who are at increased risk of impaired cognitive development. Were that feasible, intellectual assessment and special educational provisions could be arranged without delay.

This study highlights important deficits in the cognitive abilities of children with the Silver-Russell syndrome, whose IQ scores are positively correlated with their growth in head circumference. A substantial proportion require remedial educational provisions.

We would like to thank the families who assisted in this study, and in particular the Child Growth Foundation from whom a proportion were recruited. Dr Les Cox provided advice on anthropometric measurements; Jennifer Smith provided administrative assistance. Kelly Lai was supported by a Commonwealth Universities Medical Fellowship.

1 Silver HK, Kiyasu W, George J, Deamer WC. Syndrome of congenital hemihypertrophy, shortness of stature, and elevated urinary gonadotropins. *Pediatrics* 1853; **12:** 368–75.
2 Russell A. A syndrome of intra-uterine dwarfism recognizable at birth with cranio-facial dysostosis, disproportionately short arms and other anomalies. *Proc R Soc Med* 1954; **47:** 1040–4.
3 Silver HK. Asymmetry, short stature, and variations in sexual development. *Am J Dis Child* 1964; **107:** 495–513.
4 Patton MA. Russell-Silver syndrome. *J Med Genet* 1988; **25:** 557–60.
5 Tanner JM, Lejarraga H, Cameron N. The natural history of the Silver-Russell syndrome: a longitudinal study of thirty-nine cases. *Pediatr Res* 1975; **9:** 611–23.
6 Saal HM, Pagon RA, Pepin MG. Reevaluation of Russell-Silver syndrome. *J Pediatr* 1985; **107:** 733–7.
7 Davies PSW, Valley R, Preece MA. Adolescent growth and pubertal progression in the Silver-Russell syndrome. *Arch Dis Child* 1988; **63:** 130–5.
8 Tanner JM, Thomson AM. Standards for birthweight at gestation periods from 32 to 42 weeks allowing for maternal height and weight. *Arch Dis Child* 1970; **45:** 566–9.
9 Hamill PVV, Drizd TA, Johnson CL, Reed RB, Roche AF, Moore WM. Physical growth: National Centre for Health Statistics percentiles. *Am J Clin Nutr* 1979; **32:** 607–29.
10 Cameron N. *The measurement of human growth.* London: Croom Helm, 1984.
11 Jordan MD. *The CDC anthropometric software package.* Version 3. Atlanta, Georgia: Centers for Disease Control, 1986.
12 Tanner J. *Head circumference standards; birth–16 years.* Ware: Castlemead Publications, 1978.
13 Wechsler D. *Wechsler intelligence scale for children.* 3rd UK revision. Sidcup: The Psychological Corporation, 1992.
14 Neale MD. *The Neale analysis of reading ability.* Revised British edition. Windsor: NFER-Nelson, 1989.
15 Cairns E, Cammock T. Development of a more reliable version of the matching familiar figures test. *Developmental Psychology* 1978; **14:** 555–60.
16 Office of Population Censuses and Surveys. *Standard occupational classification: volume 1. Structure and definition of major, minor and unit groups.* London: HMSO, 1990.
17 Fitzhardinge PM, Steven EM. The small-for-date infant. II. Neurological and intellectual sequelae. *Pediatrics* 1972; **50:** 50–7.
18 Henrichsen L, Skinhoj K, Andersen GE. Delayed growth and reduced intelligence in 9–17 year old intrauterine growth retarded children compared with their monozygous co-twins. *Acta Paediatr Scand* 1986; **75:** 31–5.
19 Aylward GP, Pfeiffer SI, Wright A, Verhulst SJ. Outcome studies of low birth weight infants published in the last decade: a metaanalysis. *J Pediatr* 1989; **115:** 515–20.
20 Marlow N, Roberts BL, Cooke RWI. Motor skills in extremely low birth weight children at the age of 6 years. *Arch Dis Child* 1989; **64:** 839–47.
21 The Scottish Low Birthweight Study Group. The Scottish low birthweight study. II. Language attainment, cognitive status, and behavioural problems. *Arch Dis Child* 1992; **67:** 682–6.
22 Walther FJ, Ramaeker LHJ. Language development at the age of 3 years of infants malnourished in utero. *Neuropaediatrics* 1982; **13:** 77–81.
23 Washington DM, McBurney AK, Grunau RVE. Communication skills. In: Dunn HG, ed. *Sequelae of low birth weight: the Vancouver study.* Clinics in developmental medicine No 95/96. Oxford: Blackwell Scientific, 1986: 168–78.

24 Vohr BR, Garcia Coll C, Oh W. Language development of low-birthweight infants at two years. *Dev Med Child Neurol* 1988; **30:** 608–15.
25 Walther FJ. Growth and development of term disproportionate small-for-gestational age infants at the age of 7 years. *Early Hum Dev* 1988; **18:** 1–11.
26 Hawdon JM, Hey E, Kolvin I, Fundudis T. Born too small – is outcome still affected? *Dev Med Child Neurol* 1990; **32:** 943–53.
27 Wolke D. Supporting the development of low birthweight infants. *J Child Psychol Psychiatry* 1991; **32:** 723–41.
28 Chiswick ML. Intrauterine growth retardation. *BMJ* 1985; **291:** 845–8.
29 Parkinson CE, Wallis S, Harvey D. School achievement and behaviour of children who were small-for-dates at birth. *Dev Med Child Neurol* 1981; **23:** 41–50.
30 Harvey D, Prince J, Bunton J, Parkinson C, Campbell S. Abilities of children who were small-for-gestational-age babies. *Pediatrics* 1982; **69:** 296–300.
31 Villar J, Smeriglio V, Martorell R, Brown CH, Klein RE. Heterogenous growth and mental development of intrauterine growth-retarded infants during the first 3 years of life. *Pediatrics* 1984; **74:** 783–91.
32 Gareis FJ, Smith DW, Summitt RL. The Russell-Silver syndrome without asymmetry. *J Pediatr* 1971; **79:** 775–81.
33 Neligan GA, Kolvin I, Scott D McL, Garside RF. *Born too soon or born too small. A follow-up study to seven years of age.* London: SIMP with Heinemann Medical; Philadelphia: Lippincott, 1976.
34 Ounsted MK, Moar VA, Scott A. Children of deviant birthweight at the age of seven years: health, handicap, size and developmental status. *Early Hum Dev* 1984; **9:** 323–40.
35 Westwood M, Kramer MS, Munz D, Lovett JM, Watters GV. Growth and development of full-term nonasphyxiated small-for-gestational-age newborns: follow-up through adolescence. *Pediatrics* 1983; **71:** 376–82.
36 Aylward GP, Verhulst SJ, Bell S. Birth weight, gestational age, and specific dysfunction at 36 months. *Dev Med Child Neurol* 1988; **30** (suppl 57): 10–1.
37 Skuse D. The psychological consequences of being small. *J Child Psychol Psychiatry* 1987; **28:** 641–50.
38 Siegel PT, Hopwood NJ. The relationship of academic achievement and the intellectual functioning and affective conditions of hypopituitary children. In: Stabler B, Underwood LE, eds. *Slow grows the child.* London: Erlbaum, 1986: 57–71.
39 Rovet J, Netley C. Processing deficits in Turner's syndrome. *Developmental Psychology* 1982; **18:** 77–94.
40 McCauley E, Kay T, Ito J, Treder R. The Turner syndrome: cognitive deficits, affective discrimination, and behaviour problems. *Child Dev* 1987; **58:** 464–73.
41 Alley TR. Growth-produced changes in body shape and size as determinants of perceived age and adult caregiving. *Child Dev* 1983; **54:** 241–8.
42 Rotnem DL. Size versus age: ambiguities in parenting short-statured children. In: Stabler B, Underwood LE, eds. *Slow grows the child.* London: Erlbaum, 1986: 178–90.
43 Francis-Williams J, Davies PA. Very low birthweight and later intelligence. *Dev Med Child Neurol* 1974; **16:** 709–28.
44 Saigal S, Szatmari P, Rosenbaum P, Campbell D, King S. Intellectual and functional status at school entry of children who weighed 1000 g or less at birth: a regional perspective of births in the 1980s. *J Pediatr* 1990; **116:** 409–16.
45 Dunn HG, Hughes CJ, Schulzer M. Physical growth. In: Dunn HG, ed. *Sequelae of low birth weight: the Vancouver study.* Clinics in developmental medicine No 95/96. Oxford: Blackwell Scientific, 1986: 33–53.
46 Brandt I. Growth dynamics of low birth weight infants with emphasis on the perinatal period. In: Falkner F, Tanner JM, eds. *Human growth. Volume 2: postnatal growth.* New York: Plenum Press, 1978: 557–617.