Abilities and attainment in Smith-Magenis syndrome

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This study reports on cognitive abilities and attainment in 29 children and 21 adults with Smith-Magenis syndrome. There were 13 boys and 16 girls aged 6 to 16 years, and nine men and 12 women aged 16 to 52 years. All had mild to severe learning disabilities* with no differences overall between verbal and performance skills, but with a particular profile of cognitive strengths and weaknesses. Levels of attainment and of adaptive behaviour were strikingly low, and the group of adults emerged as much more dependent on carers than might have been expected from their general level of intellectual functioning. Reasons for this discrepancy are explored in terms of the severe behavioural difficulties characteristic of the syndrome.

*UK usage. North American usage: mental retardation.

Smith-Magenis syndrome (SMS) is a multiple congenital abnormality syndrome associated with learning disabilities and developmental delay. It was first described by Smith and coworkers (1982) and is believed to have an incidence of at least 1 in 25 000 births, with an equal sex ratio (Greenberg et al. 1991). The syndrome is caused by an interstitial deletion of chromosome 17p11.2 and most cases are sporadic, suggesting a low recurrence risk for parents, although at least one case of vertical transmission of the deletion from mother to daughter has been reported (Zori et al. 1993). Several candidate genes have been identified in the deleted region (Chen et al. 1996b, Elsea et al. 1996), but further research is needed to clarify their significance.

More than a hundred cases have been described in the literature, but most published reports take the form of single or small series case reports, describing variously the physical phenotype, as well as some of the commonly found behavioural and cognitive characteristics. Associated dysmorphic features reported in over two-thirds of cases include a flat, broad head, a broad nasal bridge, flat mid-face, down-turned mouth with cupid's bow, broad hands with inbent fingers, small toes, a hoarse deep voice, and short stature (Greenberg et al. 1991, 1996). With age there is a general coarsening of the facial features. Infantile hypotonia, early feeding difficulties, failure to thrive, and frequent ear infections leading to progressive hearing loss, are also common. Clinical signs of peripheral neuropathy have been found in approximately 75% of those with the syndrome, including decreased deep tendon reflexes, decreased sensitivity to pain and temperature, reduced leg muscle mass, gait disturbances, and muscle weakness (Greenberg et al. 1996). Eye abnormalities are also common, and include iris anomalies, microcornea, strabismus, cataracts, and myopia (Finucane et al. 1993, Chen et al. 1996a). Individuals with SMS are particularly prone to retinal detachment, possibly as a result of the combination of high myopia and self-injurious and aggressive behaviours (see below). Cardiac defects, renal and thyroid abnormalities, scoliosis, seizures, and genital abnormalities are less common features, found in up to one-third of those with SMS. Several adults aged in their 60s and 70s have been described in the literature (e.g. Greenberg et al. 1991), suggesting that life expectancy may be normal.

Individuals with SMS frequently pose serious management problems for their carers because of their severe behavioural difficulties. Between 50 and 100% are described as hyperactive, restless, impulsive, and distracted, and 70 to 100% are reported to show attention-seeking behaviours, temper outbursts, and aggression towards people and property (Smith et al. 1986, Greenberg et al. 1991, Dykens et al. 1997). In addition, self-injurious behaviours have been reported in between 67 and 100% of the samples investigated (de Rijk-van Andel et al. 1991, Greenberg et al. 1991, Dykens and Smith 1998). These typically take the form of hand-biting, self-pinching/scratching, picking skin around the fingernails, and tearing or pulling at the nails. Single cases have been described of children with SMS who fulfil the diagnostic criteria for autism (Smith et al. 1986, Vostanis et al. 1994), and autistic type behaviours have been reported in many cases, including resistance to change, repetitive questioning, and preoccupations with particular themes (Dykens and Smith 1998). An unusual spasmodic upper body squeeze or self-hug has been reported in 90 to 100% of affected individuals

(Finucane et al. 1994) and severe sleeping difficulties in up to 100%, including difficulties falling asleep, frequent and prolonged night waking, and early morning waking (Greenberg et al. 1996, Smith et al. 1998).

With the exception of one preliminary study (Dykens et al. 1997), there have been no systematic investigations of cognitive functioning in children or adults with SMS. It has been suggested in the literature that all affected individuals have learning disabilities (IQ<70), with the majority in the IQ range of 40 to 50 (de Rijk-van Andel et al. 1991, Moncla et al. 1991, Greenberg et al. 1996). It has been reported further that speech delay tends to be more pronounced than motor delay, and expressive language skills more impaired than receptive language skills (Chen et al. 1996b). Dykens and colleagues (1997) examined the cognitive profiles of 10 individuals with SMS and found relative weaknesses in sequential processing and in short-term memory, and relative strengths in long-term memory, alertness to the environment, attention to meaningful visual detail, and reading.

The above findings are based on small, mixed samples of children and adults, and on a range of different cognitive and developmental assessment tools. The present study aims to extend the information gathered to date by reporting findings from a systematic study of cognitive abilities and attainment in 29 children and 21 adults diagnosed with SMS. Information on levels of independence, living arrangements, and occupational activities of the group of adults will also be reported.

Method

PARTICIPANTS

The participants were drawn from two sources: membership of the British Smith-Magenis Syndrome Foundation (Parent Support Group) and all regional genetics centres in England. The centres and the support group agreed to forward letters to the families of all individuals with SMS aged 6 years and over who were known to them. The letters contained information about the study and requested permission for the child's details to be passed on to the researchers. Forty-two families were contacted via the support group, of whom twenty-eight responded and agreed to take part in the study. A further 22 positive responses were received from families via the regional genetics centres, although it was not possible to establish how many families in total had been contacted by the centres.

The final sample comprised 29 children aged 6 to 16 years, and 21 adults aged over 16 years. All had documented evidence of SMS in the form of a letter or report from a consultant clinical geneticist confirming the presence of the SMS gene deletion. Demographic details of the two groups are presented in Table I. As can be seen, in both groups the sex ratio was roughly equivalent.

Of the 29 children, the majority (n=21) were aged 6 to 11 years, with the remainder aged over 11 years. In the case of the 21 adults, the majority (n=16) were aged 16 to 28 years, with the remainder aged between 34 and 51 years. Socioeconomic status of the highest income earner in each household was determined using the Standard Occupational Classification (Government Statistical Service 1995, see Table I). In the child sample, socioeconomic status was weighted towards the higher end, with 12 families falling into the Managerial and Technical category. This is not unexpected given previous findings that members of parent support groups are predominantly middle class. In contrast, in the adult sample socioeconomic status was weighted towards the lower end, with 13 families falling into the lowest three categories. The reasons for this difference are unclear. Given that families of lower socioeconomic status are likely to have fewer resources and might therefore experience greater hardships in caring for their children with SMS, it may be that the parents of adults with SMS are particularly likely to respond to invitations to contact professionals who are knowledgeable in the field.

It is important to bear in mind that as the participant were recruited through regional genetics centres and the Smith-Magenis Syndrome Parent Support Group (both of which may be more likely to be referred individuals with significant developmental and behavioural difficulties), the present sample may well represent the more severe end of the spectrum of difficulties associated with the syndrome. There may well be less severely affected individuals who have not come to the attention of health professionals and were therefore not available for recruitment into this study.

PROCEDURE

Each child and adult was seen individually either at home or at school, college or day centre, and assessed on the following measures: (1) level of cognitive functioning was determined using the Wechsler Intelligence Scale for Children III (WISC-III; Wechsler 1992) for participants aged up to 16 years, and the Wechsler Adult Intelligence Scale – Revised (WAIS-R; Wechsler 1986) for those aged over 16 years. (2) Literacy skills were assessed using the Wechsler Reading Dimensions (WORD; Wechsler 1993). This instrument yields scores in Basic Reading (reading accuracy), Reading Comprehension, and Spelling. As the test was designed for use with children aged 6 to 16 years, age equivalent scores, derived from raw scores, were used in the analysis.

Information was also gathered from parents or other carers about the children's educational placements, and for the adults, about their living arrangements, self-care and daily living skills, as well as daytime occupations.

Results

CHILDREN WITH SMS

Cognitive abilities

The 29 participants aged 6 to 16 years were assessed on the

Table I: Demographic details

	Children (n=29)	*Adults (n=21)*
Sex		
Males	13	9
Females	16	12
Age (y)		
Mean (SD)	9.3 (2.7)	27.3 (10.7)
Range	6.3–16	16.5–51.7
Socioeconomic status		
I Professional	2	4
II Managerial/technical	12	2
III N Skilled (non-manual)	6	2
III M Skilled (manual)	4	5
IV Partly skilled	0	4
V Unskilled	1	4
VI Unemployed/home maker	4	0

WISC-III (Wechsler 1992). For seven children Full-Scale IQs fell below the basal level of 40. The IQs of the remaining 22 children ranged from 42 to 60, with a mean of 48.5 (SD 5.1). The distribution of Full-Scale IQ scores is presented in Table II. It can be seen that 22 of the participants fell into the range of severe learning disabilities (IQ of 50 or below), while seven were in the moderate learning disabilities range (IQ 51 to 70).

Considering Verbal and Performance IQs separately, nine children failed to score above the floor of the Verbal scale, and for the rest, Verbal IQs ranged from 48 to 62 with a mean of 53.9 (SD 4.5). On the Performance scale 11 children scored below the floor of the test, and the remaining children obtained IQs ranging from 47 to 64, with a mean of 52.6 (SD 5.3). There was no significant difference between the sums of scaled scores on the WISC-III Verbal and Performance scales. The comparison was repeated including only those children with a Full-Scale IQ above 40, and again there was no significant difference between scores on the two scales.

The children's performance on the individual WISC-III subtests was also examined. Table III presents the mean scaled scores for each of the 10 subtests. Within each scale, paired sample *t*-tests were performed to identify differences between subtests. As can be seen in Table IV, on the Verbal scale the mean score on the Information subtest was significantly higher than the mean scores on the Similarities, Arithmetic, Vocabulary, and Comprehension subtests. In addition, the mean score on the Similarities subtest was significantly higher than the mean scores on the Arithmetic and Comprehension subtests. Furthermore, the mean Vocabulary score was significantly higher than the mean Arithmetic score. There was no other significant difference between subtests on the Verbal scale. On the Performance scale the mean score on the Picture Completion subtest was significantly higher than the mean scores on the Picture Arrangement, Block Design, Object Assembly, and Coding subtests. The mean Picture Arrangement score was significantly higher than the mean Block Design score.

Table II: Distribution of IQ Scores on the WISC-III, child sample (n=29)

IQ	*Full-Scale* *n*	*Verbal* *n*	*Performance* *n*
40 or below	7	0	0
41 to 50	15	15	21
51 to 60	7	11	6
61 to 70	0	3	2

Table III: Mean scaled scores on the WISC-III subtests, child sample (n=29)

Verbal	*Mean (SD)*	*Performance*	*Mean (SD)*
Information	2.48 (1.77)	Picture Completion	2.97 (2.58)
Similarities	1.72 (1.19)	Coding	1.52 (0.91)
Arithmetic	1.14 (0.44)	Picture Arrangement	1.69 (1.37)
Vocabulary	1.76 (1.68)	Block Design	1.24 (0.58)
Comprehension	1.21 (0.56)	Object Assembly	1.41 (1.09)

Schooling and attainment

Most of the children (n=26) attended special needs schools that were mostly for children with moderate (IQ 50 to 69) or severe (IQ below 50) learning disabilities (Table V). Of these, six children were in residential special schools. Only three children attended mainstream schools: one was in a class for children with special needs, and the other two received extra assistance from a learning support worker for several hours each day.

Sixteen of the children obtained a score on the WORD test (Wechsler 1993) for Basic Reading and Reading Comprehension, and nine children obtained a score for Spelling. Eight children obtained scores on all three tests, while eight were readers but non-spellers; one obtained a score on the spelling test but not on the reading tests. The 16 readers had a mean chronological age of 10 years 10 months (SD 2.6 months, range 7 years 1 month to 16 years), and they obtained a mean age for Reading Accuracy of 7 years 2 months (SD 19.3 months, range 6 years to 11 years 8 months), and a mean age for Reading Comprehension of 6 years 4 months (SD 5.8 months, range 6 years to 7 years 8 months). The reading ages for Accuracy were significantly higher than the reading ages for Comprehension (t=2.47, p=0.02). The nine spellers had a chronological age of 11 years 2 months (SD 3 months, range 7 years 1 month to 16 years), and obtained a mean spelling age of 7 years (SD 15.5 months, range 6 years to 7 years 8 months).

Table IV: Differences between subtests on the Verbal and Performance scales on WISC-III, child sample (n=29)

Subtests compared	*t-test*	*df*	*p*
I > A	4.62	28	0.001
I > V	2.23	28	0.034
I > C	4.12	28	0.001
S > A	2.49	28	0.019
S > C	2.14	28	0.041
V > A	–2.27	28	0.031
PC > PA	2.74	28	0.011
PC > BD	3.86	28	0.001
PC > OA	3.44	28	0.002
PC > CD	3.47	28	0.002
PA > BD	2.10	28	0.045

I, Information; S, Similarities; A, Arithmetic; V, Vocabulary; C, Comprehension; PC, Picture Completion; CD, Coding; PA, Picture Arrangement; BD, Block Design; OA, Object Assembly.

Table V: Type of school attended, child sample (n=29)

Type of school	*n*
Mainstream	2
Remedial/special class in mainstream	1
Severe learning disabilities	10
Moderate learning disabilities	6
Mixed learning disabilities	3
Residential (learning disability)	5
Residential (autism)	1
Language unit	1

Table VI presents comparisons between the readers and non-readers, and the spellers and non-spellers, in terms of ages and IQs (scaled scores). As expected, the children who were reading and spelling were significantly older when compared with children who failed to score on these scales. In addition, the children who obtained some score on the spelling test had significantly higher Full-Scale and Verbal IQs, compared with the non-spellers. On the other hand, the readers and non-readers did not differ significantly in terms of IQ.

Finally, parents were asked whether the children showed any special abilities in terms of visuospatial skills, the use of computers, music, memory, or drawing. In 21 cases memory was rated as superior to that of even same-aged children with normal intelligence, and in a further six children memory abilities were considered superior to the child's developmental level, but not to chronological age. In particular, parents described extremely good long-term memory for past events, for example, being able to recall exact details of what someone had been wearing when the child met the person several years before. Twelve children were rated as having computer skills beyond their general developmental level, and a further four children were described as having special abilities in using computers even above their chronological age.

ADULTS WITH SMS

Cognitive abilities and attainment

Cognitive assessments were completed on 19 of the 21 adults (aged over 16 years); one adult refused to participate, saying he did not want direct contact with the investigators (although he gave consent for his carers to be interviewed), and a second adult became uncooperative halfway through the testing and refused to continue. Of the 19 adults who completed the WAIS-R, five had Full-Scale IQs below 50, and 14 had Full-Scale IQs in the range 50 to 69. One adult scored at the basal level of the test; the Full-Scale IQs of the remaining 18 adults ranged from 46 to 68, with a mean of 55.8 (SD 6.7).

Verbal IQs ranged from 51 to 71 with a mean of 58.5 (SD 5.4), and Performance IQs ranged from 48 to 74 with a mean of 60.9 (SD 7.02). There was no significant difference between Verbal and Performance IQ scores ($t=1.36$).

Mean scaled scores on the individual WAIS-R subtests are presented in Table VII. As can be seen in Table VIII, on the Verbal scale the mean scores for Vocabulary and Comprehension were significantly higher than the mean score for Information. On the Performance scale the mean scores on the Picture Completion and Object Assembly subtests were significantly higher than the mean scores on the Block Design and Digit Symbol subtests. The mean Picture Arrangement score was also significantly higher than the Digit Symbol score.

The 19 adults who completed the WAIS-R were also assessed on the WORD reading and spelling tests (Wechsler 1983). Fifteen were able to score above the basal level on Basic Reading: they obtained a mean age for Reading Accuracy of 6 years 9 months (SD 0.8 months, range 6 years to 9 years 3 months). Eleven adults obtained some score on Reading Comprehension, and had a mean Reading Comprehension age of 6 years 11 months (SD 0.8 months, range 6 years to 8 years 9 months). Fourteen adults scored above the basal level on Spelling. They obtained a mean spelling age of 6 years 6 months (SD 0.43 months, range 6 years to 7 years 3 months). There was no significant difference between scores on these subtests.

The ages and IQs of adults who were or were not able to score on the reading and spelling subtests were compared. There were no significant differences between those who did and did not score on the Basic Reading ($t=0.91$) and Reading Comprehension ($t=1.91$) subtests in terms of age. However, there was an age difference between spellers and non-spellers ($t=2.14$, $p=0.03$), with younger adults more likely to be able to spell than older adults. In addition, those adults who were able to read and to spell had significantly higher Full-Scale IQs than the non-readers ($t=2.80$, $p=0.005$) and non-spellers ($t=3.23$, $p=0.001$).

Carers were asked to report on whether the adults showed any special talents or skills. If a special skill was noted, carers were asked to rate whether in their judgement it was better than might be expected of adults of similar ages, or whether it was just above what might be expected of other adults relative to their general level of ability. For 16 of the adults memory for past events was rated as superior to that of adults with normal intelligence, and for a further three adults their memories were rated to be superior to their general developmental level. Seven adults were reported to be similarly skilled in their ability to remember verbal material. Memory for routes and special skills in using computers at a level above their developmental level were reported for four and three adults respectively.

Independence, adaptive behaviour, and occupational status

None of the adults were living independently. Just over half the sample (11 adults) were still living at home with their parents; eight were in group homes or residential communities, while two people were in residential boarding schools. Carers were asked to rate the amount of supervision the

Table VI: Ages and IQs of Readers versus Non-readers and Spellers versus Non-spellers, child sample ($n=29$)

	Readers (n=16) Mean (SD)	*Non-readers (n=13) Mean (SD)*	*p*	*Spellers (n=9) Mean (SD)*	*Non-spellers (n=20) Mean (SD)*	*p*
Age (mo)	136.8 (30.8)	92.2 (21.1)	<0.0001	138.9 (35.8)	106.9 (30.1)	0.02
Full-Scale IQ (scaled scores)	18.6 (9.4)	15.3 (5.4)	0.27	21.3 (9.9)	15.3 (6.3)	0.05
Verbal IQ (scaled scores)	8.8 (4.2)	7.7 (3.0)	0.43	10.3 (4.4)	7.4 (3.0)	0.04
Performance IQ (scaled scores)	9.8 (5.8)	7.6 (3.0)	0.22	11.0 (6.2)	7.9 (3.8)	0.11

adults required in order to perform a variety of self-care tasks and activities. Most of the adults were described as dependent on staff and requiring a high degree of support. Only three adults were able to carry out all tasks of personal hygiene independently (bathing, brushing teeth etc.); two adults were able to complete tidying up and cleaning tasks on their own initiative and without supervision; two could cook a meal on their own; and six adults were able to dress independently.

No adult was able to travel any considerable distance alone, for example to another town, although half of the group were able to move about their local area independently. Carers of 18 participants reported that they could not leave the adults alone at home for more than 1 hour, and 12 could only be left alone for a matter of minutes.

Only one adult worked in sheltered employment, as a kitchen assistant. Eight adults attended day centres or adult training centres and of these, six spent part of each week in sheltered employment on day release programmes, for example, making gift packages or sorting clothes in charity shops. A further six adults attended college courses for people with special needs, and six were still at school. None of the group had attained any formal qualifications, though a number had been awarded certificates for attending food hygiene courses at college.

Discussion

The present sample constitutes the largest cohort of individuals with SMS studied to date although, as noted earlier, it is not clear how representative the present sample is of the whole population of individuals with SMS.

All children in the present study had learning disabilities (IQ below 70) and three-quarters of the children had IQs of 50 or below, which is consistent with previous reports of the intellectual abilities individuals with SMS. In contrast, the adult sample obtained higher IQs, with 16 scoring in the range 50 to 69, and only five having IQs below 50. This difference may well be the result of real differences in the extent to which the child and adult samples gathered here are representative of the total population of affected individuals, or it may be due to a difference in the test instruments (WISC versus WAIS). Although they are regarded as equivalent, average increases ranging from 3 to 17 IQ points have been reported in various other studies in which child and adult samples have been assessed (e.g. Sattler 1982). Given the above, it is clearly not possible to conclude that individuals with SMS show an increase in IQ over time. A more appropriate conclusion is that adults with SMS do not show a decline in cognitive abilities, at least not those aged up to 50 years, and they seem to follow the same trend as the general population in showing a slight increase in IQ scores from WISC to WAIS re-testing. This is in contrast to the picture of a decline in IQ scores over time in other genetic disorders like fragile X syndrome (Hagerman et al. 1989) and Down syndrome (Dunst 1988).

As reported in a study by Dykens and coworkers (1997), long-term memory, computer skills, and perceptual skills were found to be areas of strength in both the child and adult samples, while visuomotor coordination, sequencing, and response speed emerged as areas of weakness. Such findings can help inform the planning of educational programmes for individuals with SMS. Procedures can be used to harness the individual areas of strength in teaching, for example, to encourage the use of visuospatial cues, gesture or signing, and picture symbols to support oral teaching methods. Such findings could also facilitate understanding of some of the behaviours exhibited by this group, for example, the repetitive questioning observed may be related to short-term auditory memory or sequencing difficulties identified by Dykens and colleagues (1997) and confirmed in the present study. More detailed neuropsychological investigations will be needed to clarify the cognitive profiles of children and adults with SMS.

While previous studies reported relative strengths in reading for individuals with SMS (Dykens et al. 1997), this finding was not confirmed in the present study. Only half of the sample of children was able to read at all, and although the figure rose to over three quarters in the adult sample, for both groups average reading and spelling ages were at the 6 to 7 year level. The apparent lack of progress in educational attainment from childhood to adulthood is clearly disappointing. It is not clear whether this is a function of the limited educational input provided to the adult group, or whether it reflects a ceiling of ability for individuals with SMS in the acquisition of educational skills.

The adults showed little independence in daily living skills, and were more dependent on carers than might be expected from their level of intellectual functioning. Occupational attainment was also very low, with all except one of the adults who had left school or college attending training centres or day centres rather than being in employment. The explanation for this discrepancy may lie in the high rates of severe behavioural disturbance (aggression and self-injury), poor concentration, impulsivity, attention-seeking behaviours, and autistic behaviours which characterize

Table VII: Mean scaled scores on WAIS-R subtests, adult sample (n=19)

Verbal	*Mean (SD)*	*Performance*	*Mean (SD)*
Information	1.68 (1.25)	Block Design	2.53 (1.84)
Arithmetic	2.00 (0.88)	Picture Arrangement	3.05 (1.47)
Similarities	2.32 (1.49)	Object Assembly	3.47 (2.12)
Vocabulary	2.37 (1.38)	Picture Completion	3.58 (1.71)
Comprehension	2.42 (1.07)	Digit Symbol	2.11 (1.15)

Table VIII: Differences between subtests on the WAIS-R Verbal and Performance scales, adult sample

Subtests compared	*t-test*	*df*	*p*
V > I	2.50	16	0.01
C > I	2.30	16	0.02
PC > BD	2.77	16	0.01
PC > DS	3.05	16	0.01
OA > BD	2.25	16	0.02
OA > DS	2.51	16	0.01
PA > DS	2.81	16	0.01

V, Vocabulary; I, Information; C, Comprehension; PC, Picture Completion; BD, Block Design; DS, Digit Symbol; OA, Object Assembly; PA, Picture Arrangement.

this syndrome, and which will be reported elsewhere. In other words, outcome in adulthood may be limited by the severe behavioural difficulties that are typical of SMS, rather than by cognitive level. Whatever the explanation, it is clear that educators and carers need to concentrate on helping individuals with SMS to develop their daily living and independence skills and to better use the skills and abilities they undoubtedly possess.

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