CLINICAL PRACTICE

Behaviour in mucopolysaccharide disorders

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Abstract

This paper reports a study of the nature and prevalence of behaviour problems in 258 children with mucopolysaccharide disorders. Questionnaire data obtained through the post was supplemented by home visits to 42 families in the sample and by regular discussions with families at meetings of the Society for Mucopolysaccharide Diseases. High rates of behaviour problems were found, particularly in children with Sanfilippo's and Hunter's disease aged 5 to 9 years. These included destructiveness, restlessness, and aggressiveness. Sleep problems were common across subtypes with an overall prevalence of 66%. Parents reported that they received little or no support in the management of these difficult behaviours. It is concluded that behaviour problems are a primary feature of the mucopolysaccharide disorders and place a major strain on families. Services to help families cope with these problems are urgently needed.

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While many genetic disorders are rare, cumulatively they make up a significant proportion of the disabled population of children in our society.¹ Behaviour problems in such children are common, often in association with severe developmental delay. Also there are certain behaviours in genetic disorders that are specific to the particular condition, for example the self mutilating behaviour of children with Lesch-Nyhan syndrome² and overeating in Prader-Willi syndrome.³

Identifying behaviours which are phenotypically determined in individuals with particular conditions may throw light on some of the behaviours we see in 'normal' children. Furthermore, an understanding of the natural history of these behaviours may help us develop measures of the progress of the condition and thereby provide another dimension along which to judge the efficacy of potential treatments.

In this paper we describe the behaviour problems of children with mucopolysaccharide disorders. While there are reports in the literature of high rates of behaviour problems in one subtype – Sanfilippo's syndrome^{4–6} – relatively little is known about the behavioural

Table 1 Details of the 258 children studied

Syndrome	M/F	Age (years)		Total
		Mean (SD)	Range	
Hurler's/Scheie's (MPS I)	39/24	6.5 (7.0)	0–41	63
Hunter's (MPS II)	54/–	8.6 (5.9)	0–30	54
Sanfilippo's (MPS III)	50/56	8.4 (4.2)	2–24	106
Morquio's (MPS IV)	15/20	10.3 (7.0)	0–28	35

characteristics of the other three main subtypes – Hunter's, Hurler's, and Morquio's syndromes. Elsewhere we have described the features of the early development of children with mucopolysaccharide disorders that first led parents to suspect that all was not well.⁷

Survey

The families of a total of 258 subjects completed a postal questionnaire on the development and behaviour of their affected children. One hundred and forty of these were contacted via the Society for Mucopolysaccharide Diseases (which was founded in the UK in 1982), with a further 28 being recruited mainly through the Family Fund.* In all 90 non-UK cases were recruited, mainly through families attending meetings of the Society for Mucopolysaccharide Diseases in the UK. A breakdown of the sample by sex and subtype is given in table 1. In succeeding sections we have analysed data for the 218 children aged 14 or under.

The confidential questionnaire elicited basic demographic and medical information concerning time of diagnosis and current health problems on each child. There followed a section on developmental abilities in a number of different areas based on the American Association on Mental Deficiency adaptive behaviour scale⁸ and behaviour difficulties were screened using Rutter's parent checklist.⁹ Additional information was sought on eating and sleeping behaviour and there was also space made available for comments on behaviour and general worries.

After administration of the questionnaire we visited 42 of these children, usually at home but occasionally in hospital or at school. This direct observation of the children provided us with an opportunity to check the reliability of the questionnaire with parents and to establish

*The Family Fund is an organisation funded by central government which provides financial help for families who have additional material needs as a result of having a child with a moderate or severe disability.

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Table 2 Hurler's syndrome

	Age group (years)*		
	0-4 (n=25)	5-9 (n=24)	10-14 (%) (n=49)
Abilities			
Able to walk	16	12	28 (57)
Able to speak in sentences	7	9	16 (33)
Toilet trained	3	5	8 (16)
Behaviour			
Sleep problem	16	13	29 (59)
Destructive	1	3	4 (8)
Cannot settle	12	8	20 (41)
Fearful	18	14	32 (65)
Faddy	1	4	5 (10)

*There were only two children aged 10-14 years.

its validity. Recently O'Brien has shown that a parental questionnaire, which we helped develop and which contained many similar items to our own questionnaire, was consistently and reliably answered by parents of another group of disabled children.¹⁰

HURLER'S SYNDROME (MPS I; TABLE 2)

The vast majority of children with Hurler's syndrome in this study were aged under 10 years, reflecting the severity of this particular subtype, in which survival beyond the first decade is unusual. Their mobility was compromised from early on, as compared with the other main subtypes and they were often sickly in early childhood. As a group their language abilities were quite poor although there were notable exceptions, presumably those with the milder Hurler/Scheie phenotype, who were fluent speakers, keeping up with their peers at school. Only one in eight was continent under the age of 5 years and this only rose to one in five in the 5 to 9 age group.

From a behavioural point of view, the children were often described as anxious and fearful, particularly when they were below school age, and although a proportion were somewhat restless at times, they were rarely aggressive or destructive (in contrast to the children with Hunter's and Sanfilippo's syndromes). Sleep problems were common but anecdotally the nature of the sleep disturbance exhibited was more obviously related to medical symptoms such as cough and sleep apnoea than the difficult behaviour seen in Sanfilippo's syndrome. Lastly, although many children had difficulty feeding themselves because of coordination and swallowing difficulties (obstruction from large tongue), they were not described as particularly fussy about what they ate.

Table 3 Hunter's syndrome

	Age group (years)			
	0-4 (n=13)	5-9 (n=28)	10-14 (n=7)	15-19 (%) (n=48)
Abilities				
Able to walk	12	27	5	44 (92)
Able to speak in sentences	4	12	5	21 (44)
Toilet trained	0	2	4	6 (13)
Behaviour				
Sleep problem	10	14	6	30 (63)
Destructive	9	10	1	20 (42)
Cannot settle	10	21	2	33 (69)
Fearful	12	18	5	35 (73)
Faddy	3	3	2	8 (17)

HUNTER'S SYNDROME (MPS II; TABLE 3)

The boys with Hunter's syndrome, which is the only X linked subtype of mucopolysaccharidosis, were generally more physically able than children with Hurler's disease, but this mobility, when combined with more exuberant behaviour, had implications for management as their disease progressed. Their language was slow to develop and toilet training was a problem in those under 10, although 57% of the boys aged between 10 and 14 were continent. (It should be borne in mind, however, that this older group may be less severely affected, surviving as they have done into their teens.¹¹)

As in all four main subtypes, a diagnosis of Hunter's syndrome was associated with rates of sleeping problems much higher than the rate of 14% given for a community sample of 3 year olds¹² and rates of 32% and 33%¹³ reported elsewhere for children with brain damage and mental handicap.

Overactivity was common up to the age of 10 years and aggressive/destructive behaviour seen frequently in those under 5. In several homes all breakable objects were kept out of reach and glass removed from doors, and in one case chairs were routinely lain on the floor so they could not be knocked over. Fearfulness was also characteristic of this group and most particularly of the younger boys.

SANFILIPPO'S SYNDROME (MPS III; TABLE 4)

In marked contrast with the accounts given by the other parents, those caring for children with Sanfilippo's syndrome frequently stressed the apparent normality of their early development. Coarse hair and facies were often not a feature until the child was of school age and there were several cases of strikingly attractive, fine haired children who had very severe behaviour problems. In many the children's language had developed normally initially, only to be lost over the next year or two. Thus by their early teens, fewer than one in 10 could speak fluently. As with the boys with Hunter's disease, children with Sanfilippo's syndrome were often physically quite strong with good mobility under the age of 10, which made their difficult behaviour hard to manage, particularly in public. Their incontinence was also a serious management problem.

The prevalence of behaviour problems was highest in this group. Specifically parents

Table 4 Sanfilippo's syndrome

	Age group (years)			
	0-4 (n=19)	5-9 (n=54)	10-14 (n=23)	15-19 (%) (n=96)
Abilities				
Able to walk	19	48	12	79 (79)
Able to speak in sentences	5	17	2	24 (25)
Toilet trained	0	2	4	6 (6)
Behaviour				
Sleep problem	18	46	19	83 (86)
Destructive	13	37	5	55 (57)
Cannot settle	15	38	13	66 (69)
Fearful	16	33	4	53 (55)
Faddy	1	5	1	7 (7)

described unpredictable, aggressive, and destructive behaviour and in practice this had a devastating effect on the lives of their parents. Family trips were curtailed for fear of attacks on members of the public and visits from friends reduced. Often there did not appear to be any malice intended, children would lunge at people and strike them for no apparent reason. We hypothesise that this may represent an abnormal reaction to invasion of the child's social space, leading to disturbed 'greeting' behaviour. One boy picked up rapidly at a bus stop, struck his unfortunate mother in the face and broke her nose. However, observed in his special school we noted that he caused no trouble because the other children avoided the space around him or approached him slowly. We did this and were then allowed to participate in his play.

Restlessness was common until the disease progressed to a point where mobility was limited. Children would wander round the house, upstairs and downstairs and be constantly on the move. Even when they were sitting on a sofa with someone they were likely to shout and pull the person's hair and clothes. It was difficult to take them out because they would wander off and in some cases reins were used to restrain them far beyond the age usually considered appropriate.

Also, mouthing and biting clothing and other objects was often described and seen on home visits. Some parents provided their child with a large 'teething' ring to try and reduce some of their biting behaviour. Seventy one per cent of the children aged between 5 and 14 sucked their thumb regularly.

But perhaps the most difficult area was that of sleep disturbance. Further information obtained during home visits to a number of children with Sanfilippo's syndrome, and by means of a further questionnaire completed by parents of 80 children,¹⁴ indicated that these children displayed many unusual night time behaviours such as staying up all night (45%), wandering around the house (38%), and in some cases singing and laughing in the small hours (15%). Many school age children with this syndrome were found to be sharing a room with their parents, mainly in order that they could be supervised closely, while others slept in bedrooms from which all furniture has been removed and were effectively locked in.

MORQUIO'S SYNDROME (MPS IV; TABLE 5)

Mobility in the sample with Morquio's syndrome was generally good, although the progressive nature of their skeletal deformities would be expected to lead to increasing numbers requiring artificial aids/wheelchairs in adulthood. There were problems with toilet training in the under 10 age group but four out of five of the older children were fully continent, and all except one of the 25 cases under 14 were fluent speakers.

Behaviour problems over the age of 5 were few, although four out of the 10 children aged between 10 and 14 were described as fearful. Sleep problems were present but to a lesser

degree than in the other subtypes. The only other finding of interest was the significant proportion of the children with Morquio's disease (40%) who were felt by their parents to be particularly faddy. (This compares with a rate of 13% for normal 3 year old children.¹⁵) In discussions, parents, several of whom had older children (over 10 years) with Morquio's disease reported persistent faddiness, but obviously it would be necessary to gather more information on this, and ideally make comparisons with a group of similarly disabled children, matched for age, before any claims could be made for a definitive link with the syndrome.

SUPPORT

The overwhelming majority of families in our survey had no regular help with the day to day care of their child (72%). To some extent this reflected the failure of services to meet their needs but many parents had reservations about leaving their child with someone else, either because of their child's difficult behaviour or because of their fear that they might not be there when their child died.

Parents were asked to give information on their contact with professionals in the previous year. Around 76% of families had seen a paediatrician or a general practitioner, but far fewer had seen a physiotherapist (4%), health visitor (32%) or speech therapist (31%), and less than a third had had any contact with a social worker, psychologist, education worker, or psychiatrist. Paediatric contact consisted of an annual appointment at a specialist centre, not uncommonly some distance away from home. Where contact had been made with a psychiatric unit the service offered (for example, family therapy) had sometimes seemed inappropriate when what parents wanted was advice about behaviour management. Many commented that the Society for Mucopolysaccharide Diseases, with its regular newsletters, annual conferences and support network of parents, was their main source both of support and information.

PARENTAL CONCERNS

Parents had four main areas of concern. Firstly there were many who were still very concerned about their child's prognosis which in most cases was one of deterioration leading to death. The second most common worry was about their behaviour and associated with this was

Table 5 Morquio's syndrome

	Age group (years)			
	0-4 (n=8)	5-9 (n=7)	10-14 (n=10)	0-14 (%) (n=25)
Abilities				
Able to walk	7	6	8	21 (84)
Able to speak in sentences	7	7	10	24 (96)
Toilet trained	1	2	8	11 (44)
Behaviour				
Sleep problem	3	5	3	11 (44)
Destructive	1	0	0	1 (4)
Cannot settle	2	0	0	2 (8)
Fearful	5	0	4	9 (36)
Faddy	3	1	6	10 (40)

the great distress they felt about not being able to communicate with their child in many instances. Thirdly, many children had health problems such as epilepsy, apnoea, diarrhoea, and chest infection and fourthly parents were concerned as to whether they could have further children and were desperately anxious for the latest information about antenatal screening. For all these problems parents found it difficult to get good help and advice at a local level because of the rarity of the disorder and many reported that they got most support from the parent group.

Discussion

The results of this survey strongly suggest that children with mucopolysaccharidoses display high rates of behaviour problems. These were not only higher than for the general population and for disabled groups, but also higher than for those other genetic conditions where behaviour has been studied.^{16 17} Given that these conditions are currently incurable, degenerative, and disfiguring and also that it is not uncommon for more than one child in a family to be affected, the strain on the family is clearly enormous.

We acknowledge a number of methodological flaws, particularly concerning the reliability and validity of the questionnaire. The behaviour labels, taken from the Rutter questionnaire, may have been interpreted differently in different countries and its validity for use with children under the age range for which it was designed could be brought into question. Nevertheless, the patterns of behaviour which our results suggested were subsequently confirmed to us in discussions with parents. Also, although we could have asked parents to fill out questionnaires a second time in order to gather information on reliability, we decided not to on ethical grounds as many parents found the exercise very painful, highlighting as it did the difficulties they were facing.

The fact that the study was cross sectional, as opposed to longitudinal, and that there was no control for developmental level or severity of disease, meant that while we were able to make preliminary observations on which behaviours were most prevalent in the different age groups, these data did not allow us to map out the natural history of these conditions.

Lastly, the way in which the sample was recruited may well have introduced biases. Such information as was available suggested that professional and other non-manual groups were over-represented and it is possible that parents with poor local support and/or more problems would be more likely to be members of a parent group.

Notwithstanding the above limitations, we would hope that, given the extreme rarity of these conditions which very few doctors will encounter in their careers, this study constitutes a useful addition to the literature, both on mucopolysaccharidosis and, more generally on behavioural phenotypes.

Traditionally the disorganised behaviour of children with mucopolysaccharide disorders is

ascribed to the effects of abnormal metabolites being deposited within the central nervous system. Of course the behaviours may be related to the resultant low cognitive levels of the children, but an alternative explanation is that some of these abnormal behaviours reflect more direct effects of abnormal genetic make-up. Understanding the basis of these behaviours in these unusual children may give us clues to similar behaviours seen in the normal population where it may be that many behaviours have as yet undiscovered genetic elements.

It is further hoped that this work will stimulate further research into the natural history of these distressing conditions and investigation of the ways in which they can be managed behaviourally. There is now a large body of expertise in the management of behaviour in disabled children and our experience of working clinically with a small group of children with Sanfilippo's disease with sleep problems, suggests that even a limited intervention can produce significant improvement.¹⁴

Lastly it is hoped that by disseminating information about the association between mucopolysaccharidosis and behaviour problems the chances of doctors in general practice identifying currently undiagnosed children may be increased. A significant proportion of families mentioned that difficult behaviour was the first abnormality they noticed, although sometimes it was many years before the child's condition was diagnosed. Thus some children with Sanfilippo's disease who had presented originally as overactive retarded children, were diagnosed quite late in life, by which time, sadly, they had acquired one or more similarly affected siblings. Until such time as a viable treatment is found, great emphasis needs to be placed on the need for earlier diagnosis. This would reduce the likelihood of families being faced with the awful knowledge that they have not only one, but several children with an incurable degenerative disease.

Firstly, we would like to thank parents for cooperating with our research. Their detailed observations provided the data for this paper and discussions with them about the ways they have coped with their children's behaviours have enabled us to think of strategies that we believe can help other children.

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