Psychological profile of children with Noonan syndrome

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A cohort of 48 children with Noonan syndrome, with a mean age of 9 years 10 months (SD 3y 7mo; 28 males, 20 females), was recruited from a national study. Children were assessed using the Wechsler Intelligence Scales and Test of Motor Impairment–Revised (TOMI-R). The Piers–Harris Self-evaluation Questionnaire was also completed in a subgroup of age-appropriate children. Children's parents and teachers completed the Rutter A and B scales to assess of the degree of behavioural and emotional problems respectively. Mean Full-scale IQ score was 84, and one-quarter of the participants had learning disabilities*. Verbal IQ tended to be slightly lower than Performance IQ. About half of the group showed evidence of mild to moderate impairment, confirming the impression of 'clumsiness/developmental coordination disorder' on the TOMI-R. Level of self-esteem, as determined by the Piers–Harris Questionnaire, was comparable to that of a standardized population. This research has identified some characteristic psychological features in Noonan syndrome. However, a specific behavioural phenotype could not be identified.

*US usage: mental retardation.

Noonan syndrome was described clearly for the first time in 1963 by Dr Jaqueline Noonan in children with characteristic facies, pulmonary stenosis, and short stature (Noonan and Ehmke 1963). The clinical features have been further delineated in a series of reviews (Mendez and Opitz 1985, Allanson 1987, Sharland et al. 1992, Tartaglia et al. 2001). However, studies documenting psychological aspects of Noonan syndrome are few. Anecdotal accounts of intellectual abilities and other psychological features have suggested a wide spectrum of psychological problems. For example, it has been suggested that Noonan syndrome is associated with learning disabilities, despite a lack of substantiating evidence, and parents have suggested that affected children are clumsy and have behavioural problems. In a study of 151 individuals with Noonan syndrome, Sharland et al. (1992) noted that there was a slight delay in the motor milestones and that only 11% of children of school age attended a school for children with learning disabilities, but there was no formal assessment of IQ.

So far there have only been five preliminary pilot studies looking at psychological variables in relation to Noonan syndrome. In the first two studies, Money and Kalus (1979) and Money and Dutch (1981) looked at the same eight males with Noonan syndrome, who were all between the ages of 13 and 26 years and who were recruited through a tertiary referral centre. A variety of assessment tools were used to evaluate intellectual abilities, erotosexual status, and level of behavioural problems. The findings suggested some degree of intellectual impairment. Three of the sample of eight had specific verbal and numeric reasoning difficulties. The authors also found that these males had difficulty in establishing and maintaining relationships at an age-appropriate level. Five participants had behaviour problems severe enough to merit professional help. However, the results of these studies require cautious interpretation because the sample size was extremely small.

A more recent study by Wood et al. (1995) looked at a slightly larger series of 21 children with Noonan syndrome and found a high rate of clumsiness/developmental coordination disorder, stubbornness, irritability, and communication problems. The authors did not formally measure intelligence and suggested that up to 50% of children might qualify for psychiatric help according to the behavioural scores. A Dutch study of 35 children found Wechsler Intelligence Scale for Children–Revised (WISC-R; Weschler 1974) IQs in the range of 48 to 130, with a leftward skew, and means for Full-scale IQ, Verbal IQ (VIQ), and Performance IQ (PIQ) between 86 and 89 (van der Burgt et al. 1999). Neither the study by van der Burgt et al. (1999) nor a later German postal survey study of 26 children (Sarimski 2000) found any evidence of a specific behavioural phenotype in Noonan syndrome, in spite of an overall high rate (40%) of developmental and behavioural difficulties.

Thus, overall, the understanding of the psychological functioning of individuals affected by Noonan syndrome is limited and has only been studied in a small number of affected individuals. The study described below offers further insight into the intellectual functioning and psychological profile of a group of 48 children with Noonan syndrome recruited from a national study at St George's Hospital, London, UK.

Methods

This study was designed to examine whether a pattern of intellectual functioning and psychological profile exists, and is identifiable, in children with Noonan syndrome. The study

examined the following hypotheses: That children with Noonan syndrome would have a mean IQ of 85 to 90 with a normal distribution around this mean; high rates of emotional and behavioural problems; poor gross and fine motor coordination; and low self-esteem. The study was granted ethical approval and informed consent was sought in writing from all participants.

PARTICIPANTS

Funding for the study allowed the potential assessment of about 50 participants over a 12-month period. Fifty-seven families with children aged 4 to 16 years were initially contacted from a larger cohort of 151 families involved in a large-scale genetics study. Nine families declined to participate and two families were later not contactable for unknown reasons. Thus, 46 children with Noonan syndrome, aged 4 to 16 years, were recruited from the cohort described by Sharland et al. (1992), who had been collected from a national recruitment programme involving paediatricians, geneticists, and the patient group. All participants had previously been documented in the paper by Sharland et al. (1992). At a later stage in data collection, a further two families were included due to specific requests from the parents. Therefore, the final sample consisted of 48 participant families, 46 of whom were from the original selection, and a further two participants who were included some time later.

All families received a letter which outlined the aims of the study and what would be required of them. Throughout the course of 12 months, families were contacted by telephone and appointments for home visits were arranged. Participating families lived in a geographically diverse range of locations in England. Assessments of the children were conducted at home because all families had previously travelled to St George's Hospital, London to take part in an earlier research project.

The sample consisted of 28 males and 20 females. Mean age of the whole sample was 9 years 10 months (standard deviation [SD] 3y 7mo). Types of school attended by the sample at the time of investigation were as follows: mainstream, $n=31$; mainstream with extra support, $n=8$; and special needs, $n=9$. Of the 48 children studied, 18 had received Statements of Special Education Needs or were involved in the statementing process.

Family characteristics of the cohort were recorded. In 46 of the 48 children studied, the parents were married and living together. The remaining two children were from single-parent families in which the parents were divorced and the mother remained the primary caregiver. Thirteen participants included in the study were siblings from six different families. Given the low rate of divorce in the group (4%), one might speculate that undersampling for family dysfunction might have occurred at the recruitment stage of the study.

Table I: IQ scores in 48 children with Noonan syndrome

IQ	*Mean*	*SD*
Full-scale	84.0	21.4
Visual	82.3	20.0
Performance	87.1	23.0

INSTRUMENTS

The WISC-R was used to ascertain levels of intellectual functioning in children between the ages of 7 and 16 years inclusive. The Wechsler Preschool and Primary Scale of Intelligence – Revised (Wechsler 1989) was used to ascertain levels of intelligence in children between the ages of 4 years and 6 years 11 months, inclusive.

The Rutter A and B scales (Rutter 1967; Rutter et al. 1970, 1975) were used to assess social and emotional adjustment at home and at school. The scales consist of self-report questionnaires for completion by parents (A) and teachers (B). They are scored 0 (normal), 1 (somewhat abnormal), or 2 (markedly abnormal) on a total of 26 and 20 items respectively. Total scores of 13 and 9, respectively, indicate 'child psychiatric clinic patient status'. There are at least two subscales, one of which measures 'emotional' problems and the other measures 'conduct' problems.

The Test of Motor Impairment – Revised (TOMI-R; Henderson 1987) was used to assess motor skills and manual dexterity. In the normal populations, on which this test has been standardized, most children scored 1.5 or less. 'Clumsiness' or 'Motor impairments', now often referred to as developmental coordination disorder, was inferred when TOMI-R scores were 6 or above.

The Piers–Harris Self-evaluation Questionnaire (Piers and Harris 1989) was used to assess self-esteem in children aged eight years or more. Self-esteem was not assessed in younger children, given the limited reading/conceptualizing capacity in this group.

Results

INTELLECTUAL FUNCTIONING

Full-scale IQ, VIQ, and PIQ in the cohort with Noonan syndrome are detailed in Table I. Mean level of ability on the Wechsler scales was low on all three IQ measures for children in the Noonan cohort compared to norms for a standardized population.

Table II shows the distribution of Full-scale IQ across the Noonan group. Figure 1 shows the data in graphic form. A bimodal curve is suggested, with one subpopulation showing a slight shift towards low IQ and another subgroup (about 25%) having a clearcut learning disability. However, a moderate downward shift of the whole group (with a rather even distribution around a mean IQ of 84) might have been obscured by a failure of the tests to differentiate IQs in those with severe learning disabilities, as defined by the WISC-R. Only two children had severe learning disabilities, i.e. an IQ<50.

An analysis of the differences in the VIQ and the PIQ was performed. There was a tendency towards more children having a superior PIQ than VIQ ($n=21$) than a superior VIQ in comparison with PIQ ($n=7$). Many children ($n=20$) had a PIQ approximately equal to their VIQ (within 5 points of each other; $t=-2.35, p<0.05$).

BEHAVIOURAL AND EMOTIONAL PROBLEMS

Forty-four of the participants (92% of the sample) had a score of 13 or more on the Rutter parent scale (A), indicating a disorder. Most of these (77%) had scores suggesting an emotional disorder. However, teacher scores, which were obtained for only 27 children on the Rutter teacher scale (B), did not support this conclusion. Only a small number of children (14%) showed evidence of 'clinical status' of a disorder at school.

The greater number of difficulties reported at home might be accounted for by the smaller number of questionnaires returned by the teachers or by a discrepancy between the teachers' and the parents' perceptions of the affected child.

MOTOR COORDINATION

Percentage scores for the TOMI-R test are presented in Table III. This table shows that 51% of the sample with Noonan syndrome fell into the range 6.0 or more on the TOMI-R, indicating the presence of developmental coordination disorder.

SELF-ESTEEM

Mean score (48.3, $n=30$) and SD (12.1) for children with Noonan syndrome on the Piers–Harris Questionnaire was not significantly different from those of a standardized population (mean score 51.8, SD 13.9), suggesting that children's reported self-esteem might not be affected by this syndrome.

Discussion

The results confirm that the IQ range in children with Noonan syndrome is great and that three-quarters of children with the syndrome do not have learning disabilities. Mean IQ was in the range 85 to 90, as predicted. However, many more children than expected, according to population norms, fall into the low average to 'mentally retarded' range as described by the WISC-R. Severe learning disabilities were rare in this sample. On balance, the first hypothesis of this study (normal distribution of IQ around a mean of 85 to 90) was only partly supported.

The results also suggest that some of the children with Noonan syndrome performed significantly more poorly in tests of verbal ability than in tests of non-verbal ability ($p<0.05$). This was not originally predicted. In children with discrepancies, the raw data suggested difficulties particularly in the Comprehension, Similarities, and Vocabulary subtests of the Wechsler Scales. This means that children tended to have difficulty in tasks assessing their ability to explain and elaborate aspects of the environment, whether that be the explaining of meaning of words, social standards, or similarities. The ability to 'explain' things also relies, of course, on

Table II: Distribution of Full-scale IQ (WISC-R) scores of children with Noonan syndrome ($n=48$) and standardized population

IQ	*Classification*	*Noonan*		*Standardized*[a]
		%	*n*	*%*
130+	Very superior	0	0	2
120–129	Superior	2	1	7
110–119	High average	17	8	16
90–109	Average	17	8	50
80–89	Low average	25	12	16
70–79	Borderline	12	6	7
Below 69	Mental retardation[b]	27	13	2

[a]Expected rate for standardized population. [b]UK usage: learning disability.

Table III: Mean scores from Test of Motor Impairment–Revised for children with Noonan syndrome ($n=48$) and standardized population

Score range[a]	*Noonan*	*Standardized*[b]
	%	*%*
0–1.5	7.0	55.4
2.0–3.5	25.6	29.9
4.0–5.5	16.3	9.6
6.0+	51.2	5.1

[a]Ranges are defined as follows: 0–1.5, no motor difficulty; 2.0–3.5, possible motor difficulty; 4.0–5.5, moderate motor difficulty; 6.0+, definite motor difficulty. [b]Expected values for standardized population.

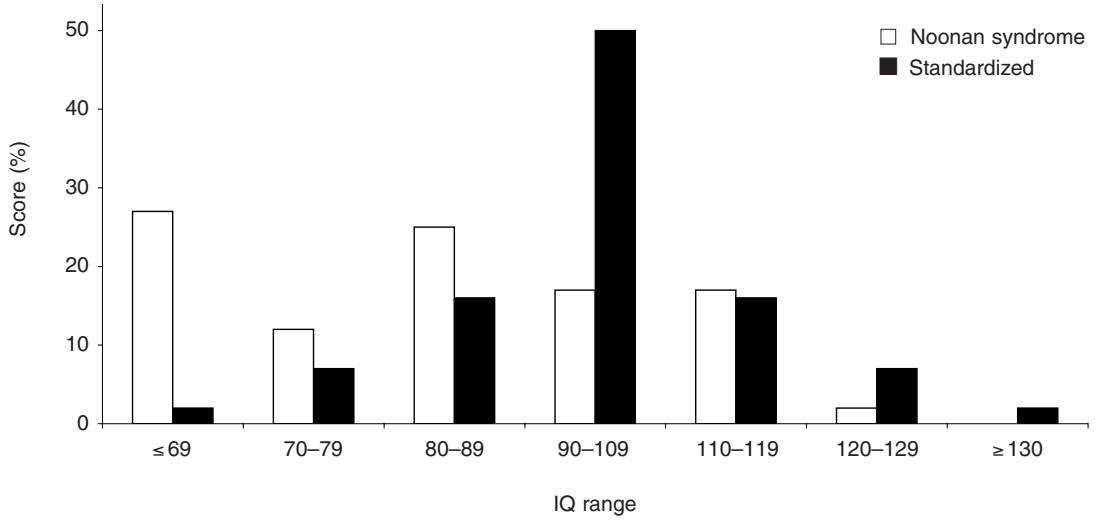

Figure 1: *Spread of Full-scale IQ scores in a population with Noonan syndrome and in a standardized population.*

overall reasoning ability and on vocabulary. Further in-depth language assessments would be required to ascertain the exact nature of the verbal difficulties shown by a subgroup of children with Noonan syndrome.

Interestingly, an examination of the raw data indicated that most of the children with Noonan syndrome performed particularly poorly on the attention subtests in comparison with the standardized sample. This finding might suggest that children with Noonan syndrome may have a tendency towards inattentive symptomatology as in attention-deficit–hyperactivity disorder.

Many parents reported that their children were 'clumsy'. The TOMI-R test results yielded strong support for this observation. Children with Noonan syndrome had a much higher incidence of suspected developmental coordination disorder than did a standardized population of equivalent age range. There was an inverse relationship between the degree of motor problems and age. Typically, clumsy children learn to adapt and manage their clumsiness but the underlying motor difficulties remain (Gillberg 2003). Perhaps this could be used to explain these observations in the study group. With respect to specific skills of manual dexterity, there might have been some improvement with age, because the older children had fewer problems than the younger ones. Clearly, practice in specific skills, such as writing, might contribute to this improvement.

As children with Noonan syndrome are usually of shorter stature than peers (Sharland et al. 1992) it might be proposed that this would affect their self-esteem in the same way that it seems to in other disorders with short stature. There was no significant difference in tests of self-esteem between data for children with Noonan syndrome and normative data.

Many parents of children with Noonan syndrome reported behaviour or adjustment problems. Most of these were classified as 'emotional' disturbance. However, teachers' reports on children's behaviour did not support a very high level of behaviour problems. A high rate of emotional problems (as suggested by the Rutter parent report), neuropsychological findings suggesting attention deficits, and a very high rate of developmental coordination disorder-like symptomatology, produce a clinical picture for these children of 'Deficits in attention, motor control, and perception', as described by Gillberg (2003). The incidence of disturbance was markedly reduced in the school environment. Not all teachers returned the questionnaires, making it difficult to compare individual children in the home and school environments. As a group, however, the incidence of social and emotional problems was much higher than one would expect to find in a standardized population.

In this study, findings on measures in the Noonan clinic sample were compared with results from normative standardization samples. It would have been preferable to study a population-representative Noonan group and a group of matched controls. Out of necessity, therefore, the design of the study limits the possibility to generalize. However, the results are based on the largest cohort so far and were drawn from a nationally recruited group of patients who have been studied in detail. In this respect the present study is probably the most representative so far.

Attempts have been made to identify specific behavioural phenotypes in some genetic syndromes (O'Brien 1992). This has been helpful in conditions such as Williams syndrome and fragile X syndrome. The information collected so far on Noonan syndrome does not support a specific behavioural phenotype. Nevertheless, verbal skills were found to be lagging behind performance skills in a subgroup of our sample (with the possibility of more specific language problems), which lends support to the findings of Wood et al. (1995) who found difficulties in language and communication. Both studies also highlighted poor motor coordination or clumsiness in most children. However, there might be a wider range of behavioural traits, and no clearly suggestive picture has emerged as yet.

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