J. Child Psychol. Psychiat. Vol. 18, 1977, pp. 297 to 321. Pergamon Press. Printed in Great Britain.

INFANTILE AUTISM: A GENETIC STUDY OF 21 TWIN PAIRS

SUSAN FOLSTEIN and MICHAEL RUTTER*
Department of Child and Adolescent Psychiatry, Institute of Psychiatry,
De Crespigny Park, Denmark Hill, London SE5 8AF

INTRODUCTION

IN HIS original description of the syndrome of infantile autism, Kanner (1943) noted that the condition was distinctive in that, in most cases, the children's behaviour had appeared abnormal right from early infancy. He suggested the presence of an inborn defect of presumably constitutional origin. Since then, there have been numerous hypotheses concerning the possible nature and origins of this defect (see Ornitz, 1973; Rutter, 1974). However, in spite of the supposition that the disorder is inborn, there have been surprisingly few attempts to investigate possible genetic influences.

The first set of evidence comes from family studies. There is no recorded case of an autistic child having an overtly autistic parent and it is decidedly unusual for a family to contain more than one autistic child, although such cases have been reported (Seidal and Graf, 1966; Verhees, 1976). The usually negative family history for autism seems to be out of keeping with genetic determination. However, this line of reasoning is fallacious. First, it is extremely rare for autistic persons to marry (Rutter, 1970) and there is only a single published report of one having given birth to a child (Kanner and Eisenberg, 1955). This fact alone invalidates the usual assumptions about the meaning of a family history. Second, autism is a very uncommon disorder, occurring in only about 2–4 children out of every 10,000 (Brask, 1967; Lotter, 1966; Wing *et al.*, 1976). If the population frequency is very low, the rate in relatives will also be low even in conditions with a high heritability (Smith, 1974; Curnow and Smith, 1975). On both these grounds a strong family history would *not* be expected even if autism was largely genetically determined.

Moreover, there are two positive findings from family history studies which *do* suggest possible hereditary influences. First, although the best available estimate indicates that only about 2 per cent of the siblings of autistic children suffer from the same condition (Rutter, 1967), this rate is 50 *times* that in the general population. Second, although a family history of autism is very rare, a family history of speech delay is much more common, being present in about a quarter of cases (Bartak *et al.*, 1975; Rutter *et al.*, 1971). This last observation raises the possibility that it is not autism as such which is inherited but rather that the genetic influence concerns some broader linguistic or cognitive impairment of which autism is but one part.

The second set of evidence comes from twin studies. These were reviewed 10 years ago (Rutter, 1967), with the conclusion that no valid inferences could be drawn. Since then, there have been several further reports (McQuaid, 1975; Kotsopoulos, 1976; Kean, 1975), but the conclusion remains the same (Hanson and

*Requests for reprints to Professor M. Rutter.

Accepted manuscript received 17 *January* 1977

Gottesman, 1976). The problems in interpretation are two-fold. First, the reports of monozygotic pairs far outnumber those of dizygotic pairs (22 compared with 10). As dizygotic pairs are twice as frequent in the general population, it is clear that there must have been serious selective biases in reporting.* This is sufficient in itself to disregard the findings. Second, excluding two pairs where the autism is associated with an overt physical disorder (Kallman *et al.*, 1940; Keeler, 1958) only five papers reporting same sexed pairs include both an adequate clinical description and evidence of zygosity (Bakwin, 1954; Kamp, 1964; McQuaid, 1975; Ward and Hoddinott, 1962; Vaillant, 1963). For what it is worth, these show two out of three concordance for monozygotic and one out of two concordance for dizygotic twin pairs. In addition, there are two opposite sexed pairs, one concordant (Kotsopoulos, 1976) and one discordant (Böök *et al.*, 1963). The great majority of the remainder report concordance in monozygotic pairs, but the papers lack either clinical details or evidence of zygosity and many are no more than passing references in publications on other topics (Chapman, 1957, 1960; Creak and Ini, 1960; Ornitz *et al.*, 1965; Polan and Spencer, 1959; Sherwin, 1953; Bruch, 1959; Keeler, 1957, 1960; Lovaas *et al.*, 1965; Lehman *et al.*, 1957; Brown, 1963; Weber, 1966; Stutte, 1960). The same problems apply to reports of twins with childhood schizophrenia (Havelkova, 1967; Cline, 1972). O'Gorman (1970) has described two monozygotic pairs concordant for "pseudo-schizophrenia" but the criteria for zygosity were not specified.

In studying genetic factors, it is necessary to bear in mind that autism is probably a behavioural syndrome with multiple aetiologies (Rutter, 1974). Certainly, it is known that the syndrome can develop in association with medical conditions as pathologically diverse as congenital rubella (Chess *et al.*, 1971) and infantile spasms (Taft and Cohen, 1971). Accordingly, the investigation of possible hereditary factors must take account of aetiological heterogeneity.

The need was apparent for a systematic and detailed study of a representative sample of twin pairs containing an autistic child. Because of the possibility that the genetic factor might apply to a broader range of disorders than autism *per se*, it would be essential to obtain detailed assessments of social, emotional, cognitive and linguistic functions in the non-autistic as well as the autistic twins. This demanded a personal study of the twins. Because twins are especially liable to suffer perinatal complications and because such complications have been thought to play a part in the aetiology of autism, it would also be necessary to obtain obstetric and neonatal data in order to check whether the concordance findings were a consequence of physical environmental factors rather than heredity. This is what we set out to do, and the present paper reports the findings.

METHODS

(a) *Subject selection*

The first task was to obtain a complete and unbiased sample of same-sexed twin pairs which included an autistic child. Opposite-sexed pairs were excluded in view of the well-established finding that autism is very much commoner in boys. A list of autistic twin pairs collected over the years by the late Dr. M. Carter provided the start. Then we sought, using multiple sources of information, to obtain information on all school age autistic twin pairs in Great Britain. Letters and personal

*Unless MZ twins were peculiarly liable to autism, which seems implausible.

14697610, 1977, 4, Downloaded from https://acamh.onlinelibrary.wiley.com/doi/10.1111/j.1469-7610.1977.tb00443.x by Universite Toulouse I Capitole, Wiley Online Library on [15/04/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

approaches were made to psychiatric and paediatric colleagues known to have a special interest in autism or who were consultants to special schools which catered for autistic children. A request for cases was also made to all members of the British Child Psychiatry Research Club. Through the Association of Head Teachers of Schools/Classes for autistic children, approaches were made to those running special schools or units for autistic children in Britain. Mrs. Monica White kindly searched the records of all children known to the National Society for Autistic Children, to identify all who were twins. A request for cases was also published in the Society Newsletter. Finally, a personal search was made, using the twin registers at the Maudsley Hospital and at the Hospital for Sick Children, London.

In this way, 33 possible pairs were identified and a detailed scrutiny was made of all available case notes and other clinical information. The sample was restricted to cases which might meet the clinical diagnostic criteria for autism outlined by Kanner (1943) and further delineated by Rutter (1971, 1977), namely, a serious *impairment in the development of social relationships* of the type characteristic of autism (that is with limited eye to eye gaze, poor social responsiveness, impaired selective bonding, a relative failure to go to parents for comfort, and, when older, a lack of empathy, a lack of personal friendships and little group interaction); together with *delayed and deviant language development* with some of the specific features associated with autism (namely poor language comprehension, little use of gesture, echolalia, pronominal reversal, limited social usage of language, repetitive utterances, flat or staccato speech and very restricted imaginative play); and also *stereotyped, repetitive or ritualistic play and interests* (as indicated by an abnormal attachment to objects, marked resistance to change, rituals, repetitive behaviour, unusual preoccupations and restricted interest patterns). Cases with an onset after age 5 years were excluded, but no further restriction was placed in terms of age of onset. Because this was a genetic study, children whose autism was associated with a known diagnosable neurological disorder (such as tuberose sclerosis or cerebral palsy) were also ruled out.

TABLE 1. SOURCE OF CASES

	Sole source	Joint source
Dr. Carter's list	1	7
National Society	0	9
Schools	0	4
Maudsley Hospital Register	2	3
Hospital for Sick Children Register	0	3
Individual psychiatrists	3	12
Newsletter advert	1	0

On the basis of information in case notes, eight twin pairs were excluded leaving a sample of 25 twin pairs to be studied in detail. After the children and parents had been seen and interviewed by one of us (SF), diagnoses were then made using all available data. At that final stage, a further four pairs were excluded, leaving a sample of 21 same-sexed pairs ranging in age from 5 to 23 years (six aged 5–9 years, eight aged 10–14 years and seven aged 15+ years). Table 1 gives the sources of selection for these 21 pairs, which constitute the basis of this paper. In a third of cases, the names were available from just one source, but most cases were notified by several different sources. It is clear that no one source would have been adequate.

(b) *Zygosity*

Zygosity was determined by physical appearance, fingerprints and blood grouping. Attention was paid to such detailed physical characteristics as eye colour and pattern of iris; hair colour, texture and curliness; and shape of nose, ears and hands as well as general appearance (Gedda, 1961). In eight of the pairs, the differences between the twins were sufficiently marked to be sure of dizygosity without the need for further testing. In two pairs, a designation of monozygosity was made on the basis of very close physical similarity plus the results of fingerprint analysis using the ridge count method described by Holt (1961). Blood groups testing (Race and Sanger, 1975) was undertaken for 12 pairs,* nine of which proved to be monozygotic. Thus, the sample consists of 11 monozygotic and 10 dizygotic pairs.

*In two pairs, the blood tests showed that the parents' view of zygosity was wrong.

14697610, 1977, 4, Downloaded from https://acamh.onlinelibrary.wiley.com/doi/10.1111/j.1469-7610.1977.tb00443.x by Universite Toulouse I Capitole, Wiley Online Library on [15/04/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

(c) *Data collection*

In all cases, an attempt was made to interview the parents, using a standardized interview and also to interview and examine both twins. Complete information was obtained in 19 pairs. In one case, the parents and the autistic twin were interviewed but the normal twin was not seen, in a second no interview was undertaken. However, in both cases where personal interviewing was incomplete, the children had been previously studied very extensively and detailed descriptions, findings and photographs were made available to us.

Topics covered in detail by the parental interview included a systematic account of the children's social, emotional and behavioural development and present status; language development, competence and characteristics; early history and developmental milestones; account of pregnancy, labour and perinatal period; illnesses and separations; family characteristics and social circumstances; and family history of psychiatric and neurological disorder. Vineland Social Maturity Scale (Doll, 1947) and Mecham Language Scale (Mecham, 1958) assessments were also undertaken.

The children were closely observed and interviewed at home or in hospital and all were given a detailed neuro-developmental examination. If systematic psychological test findings were not readily available, further testing of cognition and language was undertaken using the Wechsler (1949), Merrill–Palmer (Stutsman, 1948) and Reynell (1969) scales.

Paediatric and psychiatric case records were obtained and studied for all hospital admissions and attendance. Finally, hospital obstetric records were examined for all but one of the 17 twin pairs born in hospital.

(d) *Diagnosis of autism*

Systematic biases readily arise in twin research through the possibility of the psychiatric diagnosis of one twin being influenced by knowledge on his co-twin and on the zygosity of the pair. Accordingly, rigorous precautions were taken in the study to ensure that such diagnostic contamination could not occur. The procedure was as follows. First, one of us (S.F.) prepared a detailed separate summary of all available psychiatric and developmental information for each of the twin children included in the study. These summaries were then carefully scrutinized to ensure that all possible identifying information (such as family characteristics) were deleted. As a further precaution, the age of the child was given only in terms of a 5-year grouping. The case histories were then put into random order and given a new case number so that it was no longer possible to sort by pairs. These randomized case histories without identifying information were then given to the other investigator (M.R.) for diagnosis, made "blind" both to pair and to zygosity. His diagnoses are those used for the purposes of all analyses.

Autism was diagnosed on the basis of the strict criteria already outlined. As noted, at this stage, the sample was reduced to 21 pairs including 25 autistic children as a result of these "blind" diagnoses. Fourteen children were diagnosed as showing typical and characteristic infantile autism.* A further 11 met the criteria for autism, but the clinical picture was somewhat atypical in some way. Thus, in one child the onset was not until the age of $3\frac{1}{2}$ years; in another child the course was unusual in that almost all autistic features were lost by the age of 6 years (interestingly, he was otherwise fairly typical except that an air encephalogram showed cortical atrophy); and other children were atypical in terms of more social responsiveness or less ritualistic activity than usual.

A separate diagnosis of cognitive/linguistic impairment was made on the basis of at least one of the following features: lack of phrase speech by 30 months, a verbal I.Q. or social quotient of 70 or below, grossly abnormal articulation persisting to age 5 years or older and scholastic differences of such severity as to require special schooling. All 25 autistic children met at least two of these criteria and a further six non-autistic children also did so.

Finally, a psychiatric assessment was made with respect to any non-autistic disorders which were present. In view of its possible connection with infantile autism, particular attention was paid to the possible presence of so-called "autistic psychopathy" meaning a condition characterized by gross social impairment, obsessive preoccupations or circumscribed interest patterns and poor coordination but normal general intelligence (van Krevelen and Kuipers, 1962; van Krevelen, 1963).

*The original "blind" diagnoses gave only 12 cases, but further information made available later on one concordant pair caused them to be transferred from the atypical to the typical category. This change does not affect the concordance findings.

14697610, 1977, 4, Downloaded from https://acamh.onlinelibrary.wiley.com/doi/10.1111/j.1469-7610.1977.tb00443.x by Universite Toulouse I Capitole, Wiley Online Library on [15/04/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

DESCRIPTION OF SAMPLE

(a) *Typical–atypical differentiation*

In view of the uncertainty whether the typical–atypical differentiation had any validity or meaning, the clinical features of these two subgroups were systematically compared (see Table 2). Very few differences were found apart from the items which

TABLE 2. COMPARISON OF TYPICAL AND ATYPICAL CASES

	Typical (n=14)	Atypical (n=11)
% male	72	81
% social class I & II	43	55
% biological hazards	57	36
Mean I.Q.	52·9	61·4
Mean lang. abn. score*	5·0	4·3
Mean social abn. score†	4·6	3·0
Mean repetitive behav. score‡	3·7	3·0

*Based on six items: lack of use of gesture, echolalia, steteotyped speech, repetitive speech, lack of social use of speech, abnormal mode of delivery (nine non-speaking children omitted from this analysis).

†Based on five items: lack of social smiling in first year, lack of eye to eye gaze, lack of attachment to parents, abnormal relationship with peers, lack of empathy.

‡Based on five items: abnormal attachment to objects, resistance to change, stereotyped play or interests, rituals, repetitive movements.

led to the group being classified as atypical. Thus, there were no marked differences in terms of sex, I.Q., language abnormalities or social class, and there were only marginally fewer repetitive and stereotyped symptoms. The main difference was that the atypical children showed less severe social abnormalities and four of them had an onset after 30 months (by definition none of the typical children had such a late onset). Also, biological hazards were slightly (but not significantly) less common in the atypical group. In view of the fact that, in most respects, the typical and atypical children were so similar, these two subgroupings are combined in presenting the results.

(b) *Comparison with non-twin samples*

The 21 twin pairs gave rise to 25 cases of autism. As is evident from Table 2 and from the case histories in the Appendix, the behavioural characteristics of the autistic twins were closely comparable to non-twin samples. Table 3 shows how other features compare with a study of singletons previously undertaken by one of us (Rutter *et al.*, 1967).

Of the 25 autistic children, 19 were male, giving a male : female ratio of 3·1 to 1 which is similar to most other studies. The parents came from all social strata but were predominantly middle class, which is in line with most other series. Other family characteristics were also much as expected. Thus none of the parents suffered from schizophrenia and only one (case 19) of the 36 sibs was autistic (a rate of 2·8%). However, in three of the 21 families (14%) either a parent or sib had experienced a severe delay in the acquisition of spoken language (cases 2, 10 and 14).

14697610, 1977, 4, Downloaded from https://acamh.onlinelibrary.wiley.com/doi/10.1111/j.1469-7610.1977.tb00433.x by Universite Toulouse 1 Capitole, Wiley Online Library on [15/04/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

TABLE 3. SEX, I.Q. AND SOCIAL CLASS

	Twins (this study)	Singletons (Rutter *et al.*, 1967)
Sex ratio	3·2 : 1	4·25 : 1
I.Q.		
< 50	48·0%	43·0%
50–69	20·0%	28·5%
70+	32·0%	28·5%
Social class		
I and II	57·0%	55·5%
III	28·5%	41·3%
IV and V	14·5%	3·2%

About half the autistic children were severely retarded, but nearly a third had an I.Q. in the normal range on non-verbal tests, which again is closely comparable to other findings. By definition, none of the children had a diagnosable neurological condition. However, two-thirds showed impairment on developmental functions such as motor coordination or had isolated minor signs such as strabismus or choreiform movements. Four of the autistic children had developed epileptic fits during adolescence. In 11 cases, EEGs had been reported as abnormal, but, in most cases, the abnormalities were of a non-specific nature. Air encephalograms had been undertaken in three children; these showed left-sided cortical atrophy in one case, slight dilatation of the right lateral ventricle in a second case and no abnormality in a third. It may be concluded that, apart from the fact that they are twins, the 25 autistic children in the sample are closely similar to the autistic children described in non-twin populations.

RESULTS

(a) *Concordance for autism*

Of the 10 dizygotic twin pairs, *none* was concordant for autism, whereas *four* of the 11 monozygotic pairs were concordant (Exact test; $P = 0{\cdot}055$). This gives

TABLE 4. PAIRWISE CONCORDANCE BY ZYGOSITY

	MZ pairs ($n = 11$)	DZ pairs ($n = 10$)	MZ–DZ difference (Exact test)
	(%)	(%)	
Concordance for autism	36	0	$P = 0{\cdot}055$
Concordance for cognitive disorder (including autism)	82	10	$P = 0{\cdot}0015$

a 36% concordance rate by pair or a 53% concordance rate by proband for MZ pairs and in each case a zero per cent concordance for dizygotic pairs [see Gottesman and Shields (1976) for a discussion of concordance by pair or by proband].

Two of the concordant MZ pairs (1 and 3*) were closely similar in all respects. In each case, the twins were severely retarded and the autism was somewhat atypical

*Numbers refer to case summaries in the Appendix.

14697610, 1977, 4, Downloaded from https://acamh.onlinelibrary.wiley.com/doi/10.1111/j.1469-7610.1977.tb00443.x by Universite Toulouse I Capitole, Wiley Online Library on [15/04/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

in terms of the limited evidence of ritualistic features. However, in both the other two pairs, there were important differences between the twins in spite of concordance for autism. In one (2) there was an 18 point difference in non-verbal I.Q. and a 24 point difference in Peabody language quotient. The twin with a lower non-verbal I.Q. but higher verbal I.Q. made much more progress in both social relationships and use of language. In the fourth pair (4) there was a 39 point I.Q. difference; in this case, the more intelligent twin was less severely autistic, although the type of behaviour was closely similar in both. It is also notable that the more intelligent twin did not develop autism until 3 years of age, although apart from the late onset the clinical picture was typical of autism.

(b) *Concordance for cognitive or social impairment*

The next question is: what is inherited? Is it autism as such or is it some broader form of which autism is but one part? To answer this it is necessary to examine the pattern of disabilities in the non-autistic co-twins and to determine the concordance in MZ and DZ pairs for these disabilities.

In addition to the 25 autistic children, another six showed some form of cognitive impairment. In all cases, this involved some kind of speech or language deficit but the type of deficit varied. Three of the six children (cases 5, 8, and 12) had been markedly delayed in early speech development, not using phrase speech until 3 years or later. One of these (5) was also mildly retarded and attended a special school. A further child had markedly abnormal articulation to age 7 years, although she had not been delayed in early speech development. Another child (case 9) with SQ of 70 had been generally mildly retarded in development and did not use phrase speech until 28 months. The sixth child (case 6) had a verbal I.Q. 21 points below the non-verbal and attended an ESN school but there had been no speech delay.

Five of the six children with cognitive impairment were in MZ pairs. Thus, five of the seven non-autistic children in MZ pairs had cognitive abnormalities compared with only one of the 10 non-autistic children in DZ pairs (Exact test; $P = 0{\cdot}0175$). As all the 25 autistic children also met the criteria for cognitive abnormality, the concordance rates may be recalculated for all forms of cognitive impairment, both autistic and non-autistic (see Table 4).

The results are striking. Nine of the 11 MZ pairs were concordant for some kind of cognitive disability, usually involving language, whereas this was so for only one out of the 10 DZ pairs (Exact test; $P = 0{\cdot}0015$).

Only one child (case 8), included in the six just mentioned, had social or behavioural problems at all reminiscent of autism, and he was diagnosed as showing autistic psychopathy on the basis of little social usage of speech, circumscribed interest patterns and a lack of social relationships.

Three of the other children with cognitive impairments, however, also showed some kind of social or emotional disability. One child (7) was painfully sensitive and self-conscious, crying over imagined slights; another (6) although friendly and sure of himself now, had had a severe and disabling dog phobia when younger, and a third (5) was rather shy, sensitive and lacking in confidence. A fourth child (13) without cognitive impairment developed a psychiatric disorder of uncertain nature at age 17 years. Because of the overlap with cognitive impairment, the concordance

14697610, 1977, 4, Downloaded from https://acamh.onlinelibrary.wiley.com/doi/10.1111/j.1469-7610.1977.tb00433.x by Universite Toulouse 1 Capitole, Wiley Online Library on [15/04/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

in terms of social/emotional difficulties (including autism) is similar: eight out of 11 MZ pairs compared with two out of 10 DZ pairs.

(c) *Biological hazards and concordance*

The major difference in concordance between MZ and DZ pairs strongly suggests the importance of hereditary influences in the aetiology of autism. However, before drawing that conclusion it is necessary first to check whether the concordance patterns are explicable in terms of biological hazards associated with the birth process. We identified five features known to be associated with brain damage (and hence likely to predispose to autism): severe haemolytic disease (Gerver and Day 1950), a delay in breathing of at least 5 minutes after birth (Drage and Berendes, 1966; Hunter, 1968), neonatal convulsions (Rose and Lombroso, 1970), a second birth which was delayed by at least 30 minutes following the birth of the first twin (Dunn, 1965; Kurtz *et al.*, 1955) and multiple congenital anomalies. Such features were present in 11 out of the 42 children.

TABLE 5. CONCORDANCE/DISCORDANCE FOR AUTISM BY PRESENCE OF BIOLOGICAL HAZARDS

	Biological hazards		
	Both twins	One twin only	Neither twin
Concordant	0	1	3
Discordant	2	6	9

Table 5 shows the concordance for autism in terms of biological hazards. In only two pairs, did both children experience biological hazards and both these pairs were *dis*cordant for autism. It may be concluded that the concordance is likely to be due to genetic factors and certainly is not explicable in terms of the perinatal complications on which we had data, and the same applies to the concordance for cognitive impairment. In *none* of the six pairs concordant for cognitive impairment but not autism were biological hazards present in both twins.

(d) *Biological hazards and discordance*

The next question is why only some of the children with a cognitive impairment showed the syndrome of autism. The possible importance of biological hazards in this connection was re-examined by focusing on the 17 pairs discordant for autism. In six of these pairs one, but only one, of the twins had experienced one of the five specified biological hazards. In *all six* cases, it was the autistic twin who was affected (see left-hand side of Table 6). However, there were a further 11 cases (see right-

TABLE 6. BIOLOGICAL HAZARDS AND DISCORDANCE FOR AUTISM

	Biological hazards			
	Autistic twin only	Other twin only	Both twins	Neither twins
MZ pairs	2	0	0	5
DZ pairs	4	0	2	4

14697610, 1977, 4, Downloaded from https://acamh.onlinelibrary.wiley.com/doi/10.1111/j.1469-7610.1977.tb00443.x by Universite Toulouse I Capitole, Wiley Online Library on [15/04/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

hand side of Table 6) in which the biological hazards affected neither twin or both twins, and so did not account for the discordance.

TABLE 7. BIOLOGICAL DIFFERENCES AND DISCORDANCE FOR AUTISM

	Biological differences		
	Autistic twin worse	Other twin worse	No difference
MZ pairs	2	0	3
DZ pairs	4	0	2

In order to examine these 11 discordant cases further, a wider definition of biological hazard, in terms of a marked difference between the twins, was employed. This included a birth weight at least a pound less than the other twin (three cases) (Willerman and Churchill, 1967), a pathologically narrow umbilical cord (one case), a more severe haemolytic anaemia associated with neonatal apnoea (two cases), and a severe febrile illness possibly involving encephalitis (one case).This differentiated a further six cases (see Table 7), and again it identified the autistic one each time. It may be concluded that some form of biological impairment, usually in the perinatal period, strongly predisposed to the development of autism. The pattern of findings is summarized in Table 8.

TABLE 8. SUMMARY OF BIOLOGICAL HAZARDS IN DISCORDANT PAIRS

Hazard	Autistic twin	Non-autistic twin
	MZ PAIRS	
Definite	Multiple congenital anomalies	—
	Neonatal convulsions	
Possible	Severe febrile illness	—
	Pathologically narrow cord	—
None	—	—
	—	—
	—	—
	DZ PAIRS	
Definite	Apnoea	—
	Delay second birth	—
	Delay second birth	—
	Delay second birth	—
Possible or Difference in severity	Severe haemolytic disease + apnoea	Delay second birth
	Severe haemolytic disease + apnoea	Mild haemolytic disease
	Birth weight $1\frac{3}{4}$ lb lower	—
	Birth weight $1\frac{3}{4}$ lb lower	—
None	—	—

Did the same biological hazards explain the presence of a cognitive deficit? To examine this question, we compared the six non-autistic twins who showed

14697610, 1977, 4, Downloaded from https://acamh.onlinelibrary.wiley.com/doi/10.1111/j.1469-7610.1977.tb00443.x by Universite Toulouse 1 Capitole, Wiley Online Library on [15/04/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

cognitive impairment with the 11 non-autistic twins without a cognitive deficit. The only two children (out of these 17) who had experienced a biological hazard were both *without* a cognitive disability. Clearly, biological hazards did *not* account for the presence of cognitive abnormalities.

(e) *Psychosocial influences*

The final issue was whether psychosocial environmental influences were associated with discordance in terms of either autism or cognitive impairment. Because both were evident from early life, it was necessary to focus on possible factors in the infancy period, which meant that our data were necessarily retrospective in large part and often crude. All pairs had been reared together during infancy, although in one case (11) the autistic child was often in hospital during the first year. In this case, the severe early lack of responsiveness was followed by maternal rejection. There were no differences between the autistic and non-autistic children in experiences other than those which were associated with the greater frequency of neonatal biological hazards. Thus, out of the nine cases in which there was a difference in time before discharge home after birth, in seven it was the autistic child who stayed in hospital longer. In some instances, this involved periods in an incubator or some kind of intensive care.

DISCUSSION

(a) *Sampling and selection*

Before discussing the meaning of the findings it is necessary to consider the adequacy of our sampling, as the rest of the results hinge on that. In order to obtain as complete a sample as possible we used an unusually large number of sources of diverse kinds. As a result, most of the children were reported by several different agencies. This in itself provides some indication of the efficiency of our sampling techniques. However, two better checks are available. First, there is the monozygotic–dizygotic pair ratio. For same-sexed pairs surviving the first year, the ratio should be approximately 6 : 7 (Slater and Cowie, 1971), which is very close to our observed ratio of 11 : 10. Second, there is the number of autistic twins found. The Registrar-General figures for 1964 show that 6176 liveborn same-sexed twins were born that year (Slater and Cowie, 1971). Taking a 1-year survival rate of 88·1% (based on Gittelsohn and Milham's 1965 figures) that reduces to 5441. Our sampling was most thorough for the school years so if we multiply that by 13 to obtain the figure for the birth years 1958–1970 that makes 70,733 pairs and 141,466 children. The next step is to calculate the proportion of autistic children expected. We had to rely on information about children referred to clinics or special schools *and* diagnosed as autistic by them and later also by us. For this purpose, the administrative surveys probably provide the most appropriate initial guide. In Britain, the Department of Education figures showed a prevalence of 1·75 per 10,000 (Wing *et al.,* 1976) and in the U.S.A. Treffert's (1970) figure was 2·5 per 10,000. On this basis, we should have had between 24·8 and 35·4 children. However, as with other studies (Wing *et al.,* 1976), we found that not all the cases reported as autistic met our diagnostic criteria. In practice, we excluded about a quarter, which brings the expected number of twins in our final

14697610, 1977, 4, Downloaded from https://acamh.onlinelibrary.wiley.com/doi/10.1111/j.1469-7610.1977.tb00443.x by Universite Toulouse I Capitole, Wiley Online Library on [15/04/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

sample down to 18·6 to 26·6.* In fact (excluding the four children born before 1958 and the one living in Scotland) we obtained 20 autistic children who were part of a same-sexed pair—which is very close to the expected number. It may be concluded that there is every reason to believe that our sample of autistic twins was about as complete as it could be.

It is also necessary to consider whether the choice of a twin sample introduced any particular biases. The most obvious possibility concerns the frequency of perinatal complications. These tend to be rather commoner in multiple births than in single births (Dunn, 1965) and this may have increased the likelihood of our finding an association between birth hazards and autism. On the other hand, studies of singletons have also suggested that perinatal complications tend to be somewhat commoner in autistic children than in other children (see e.g. Lotter, 1967; Whittam *et al.*, 1966; Hinton, 1963; Moore, 1972; Knobloch and Pasamanick, 1974; Torrey *et al.*, 1975), although not usually to the extent found in this twin sample. It should be noted, however, that our sample did not have particularly low birth weights. Thirty of the 42 children had a birth weight of over 5 lb and none had a birth weight under 3 lb. We may conclude that our choice of a twin sample probably increased the likelihood of finding an association between perinatal complications and autism, but similar associations of lesser degree have been noted in singletons.

Similarly, it is well known that delayed acquisition of speech is commoner in twins than singletons. It might be suggested that this is why so many of the non-autistic twins showed impaired language. However, were this simply due to twinning, it would be expected to occur with equal frequency in the MZ and DZ pairs (Mittler, 1971). In fact, we found that abnormalities of language were much more frequent in the MZ than in the DZ twins. Moreover, the abnormalities we found did not consist of just speech delay but rather involved a wider range of cognitive functions.

Finally, there is the question of sample size. How much confidence can be placed on the MZ–DZ differences in concordance in view of the relatively small sample size of 21 pairs? Obviously, some caution is needed before drawing too sweeping conclusions, and clearly replication is required. Nevertheless, as already indicated, there are good reasons for supposing that this twin study has avoided the serious biases which plague twin research. Moreover, although the sample is small, the MZ–DZ differences were large and statistically significant. It seems likely that the concordance differences are true ones.

(b) *Hereditary influences*

The MZ–DZ difference in concordance for autism and the much larger difference in concordance for cognitive disorder clearly points strongly to the importance of genetic factors in the aetiology of autism. Indeed, the size of the MZ–DZ difference, together with the population frequency of autism indicate a very high heritability or coefficient of genetic determination (Smith, 1974; Curnow and Smith, 1975). The finding that concordance is strongly associated with the zygosity of the twin pairs

*However, using Lotter's (1966) true prevalence figures and also a broader definition of autism than we employed, there should be 63 autistic twins in the country who could be identified by means of a population survey.

14697610, 1977, 4, Downloaded from https://acamh.onlinelibrary.wiley.com/doi/10.1111/j.1469-7610.1977.tb00443.x by Universite Toulouse 1 Capitole, Wiley Online Library on [15/04/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

and not at all with the presence of physical environmental hazards indicates that the concordance truly represents an hereditary influence rather than biological damage during the birth process. In this connection, it should be noted that there are *greater* intra-uterine environment differences in MZ than in DZ pairs, as reflected, for example, in the greater mean difference in birth weights in MZ pairs (Mittler, 1971).

(c) *What is inherited?*

The findings clearly point to the conclusion that the hereditary influences are concerned with a variety of cognitive abnormalities and not just with autism. In other words, autism is genetically linked with a broader range of cognitive disorders. The results also show that the cognitive deficits linked with autism usually involve delays or disorders in the acquisition of spoken language. Thus, of the six pairs concordant for cognitive impairment, in three the non-autistic twin was not using phrase speech until after his third birthday. One of the remaining three showed a lesser degree of speech delay, a second had verbal skills much inferior to visuo-spatial, and the third had very abnormal articulation. It may be inferred that language difficulties of some kind are generally part of the problem. The conclusion is in keeping with the extensive evidence for the importance of abnormalities in language and symbolization in autism (Rutter, 1974).

On the other hand, in most of the non-autistic children, it was not usually a straightforward isolated developmental delay in language acquisition. First, two of the six children also had some general intellectual impairment. Second, in one case, the language delay involved echolalia, and in another it involved a lack of social usage comparable to that found in infantile autism. It seems that a language deficit may be a part of the cognitive impairment in most cases but it is not usually a "pure" or isolated delay in the acquisition of spoken language. Of course, it is not suggested that all forms of language impairment are genetically linked to autism. Indeed, in most respects, the language characteristics of autistic children are very different to those of children with a developmental language disorder (Bartak *et al.*, 1975, 1977). However, it seems that *some* cases of language abnormality are genetically linked with autism. Unfortunately, knowledge is lacking on how to tell which these are.

It is also necessary to ask whether the social and emotional difficulties which were present in most of the children with a cognitive deficit are also part of what is inherited. For several reasons, no firm conclusions are possible on this point. In the first place, social difficulties and emotional disturbance are quite common in any group of children with language delay (Rutter, 1972; Stevenson and Richman, 1977), and with a sample as small as ours it was not possible to determine whether difficulties were more common in this group. In the second place, only one of the six children with cognitive impairment had social difficulties of a kind at all similar to those shown by autistic children. It may be that the shyness, fears and sensitivity are part of what is inherited or it may be that, as in other children with language delay, they are merely temporary secondary emotional reactions to cognitive and communication difficulties. The present data do not allow a choice between these two possibilities.

14697610, 1977, 4, Downloaded from https://acamh.onlinelibrary.wiley.com/doi/10.1111/j.1469-7610.1977.tb00443.x by Universite Toulouse I Capitole, Wiley Online Library on [15/04/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

A twin study could provide the opportunity to examine possible links between autism and schizophrenia. However, very few of the twins in this sample were old enough to determine whether autism and schizophrenia ever occur together in monozygotic pairs. None of the monozygotic twins had a disorder with any resemblance to schizophrenia. But there was one non-autistic dizygotic twin who showed social withdrawal at age 17 years. The possibility of schizophrenia clearly arises, but there was no evidence of thought disorder, delusions, hallucinations or any other first rank symptoms. Further follow-up is needed to make a diagnosis. Nevertheless, it should be added that, in spite of a large number of twin studies of schizophrenia, no case has ever been reported of infantile autism occurring in a non-schizophrenic co-twin.

(d) *Mode of inheritance*

It is obvious from the low rate of disorder in the sibs that autism is not a disease inherited in clear-cut Mendelian fashion. However, many factors (e.g. phenocopies, genetic heterogeneity, incomplete penetrance, high mutation rate, etc.) may distort the simple Mendelian ratios. In practice, it is extremely difficult on the basis of family data to differentiate between monogenic inheritance with incomplete penetrance and polygenic or multifactorial effects (Curnow and Smith, 1975). In the case of autism, the sorting out of mode of inheritance is much complicated by the fact that autistic children rarely marry and have children. One crucial piece of information which is needed is what happens to the offspring of non-autistic sibs or twins with cognitive impairment. Unfortunately, no information is available on that point and until this is known genetic model building seems premature.

(e) *Environmental influences*

Our findings clearly indicate that, in addition to hereditary factors, environmental hazards involving the risk of brain damage also play an important part in the aetiology of autism. Out of the 17 pairs discordant for autism, there were 12 in which autism was associated with some kind of biological hazard or difference which affected the autistic child and not his co-twin. In this series, with one exception, the biological features were all perinatal in origin. However, it is clear from studies of non-twin samples that autism may arise on the basis of quite diverse forms of brain pathology, including congenital rubella (Chess *et al.*, 1971) and infantile spasms (Taft and Cohen, 1971).

Although both hereditary and environmental influences play an important part in the genesis of autism, the findings from this study suggest that they work in rather different ways. The MZ–DZ concordance differences showed that the hereditary factor(s) were concerned with the genesis of cognitive/linguistic abnormalities rather than with just autism as such. But this was not the case with the biological hazards at all. They were completely *un*associated with non-autistic cognitive deficits in spite of a strong association with autism.

(f) *Genetic–environmental interactions*

That difference raises the question of how far hereditary and environmental influences cause different cases of autism and how far they act in conjunction as part

14697610, 1977, 4, Downloaded from https://acamh.onlinelibrary.wiley.com/doi/10.1111/j.1469-7610.1977.tb00443.x by Universite Toulouse 1 Capitole, Wiley Online Library on [15/04/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

of a multifactorial determination. Our data do not allow any firm conclusions on this point but they suggest that both occur.

The four MZ pairs concordant for autism suggest that, in some cases, genetic factors may be sufficient to cause autism. Only one of the eight autistic children in these four pairs suffered a hazard at all likely to lead to brain injury—his disorder was more severe than that of his co-twin.

On the other hand, it appears that brain injury alone may also be a sufficient cause of autism. This is suggested by the fact that biological hazards occurred with much the same frequency in MZ and DZ pairs. It is also indicated by the finding from other studies that the rate of autism in children with particular forms of brain pathology, such as caused by congenital rubella (Chess *et al.*, 1971) is considerably higher than that in the sibs of autistic children.

Nevertheless, many cases of autism appear to result from a combination of brain damage and an inherited cognitive abnormality. This is suggested by the finding that out of the seven MZ pairs discordant for autism, in four cases the autistic child but not his non-autistic co-twin had experienced some form of biological hazard liable to cause brain damage. In three of these four cases the non-autistic child had a cognitive deficit, suggesting that it may have been brain injury that converted the deficit into a full-blown autistic syndrome.

In this regard it is interesting that, over a decade ago, van Krevelen (1963) suggested that autism might result from the combination of an inherited personality deficit plus organic brain damage. The present results are in accord with that general hypothesis, but the deficit found involved cognitive/linguistic abnormalities rather than the "autistic psychopathy" syndrome postulated by van Krevelen.

In summary, we may conclude that this systematic study of 21 same-sexed twin pairs in which at least one twin showed the syndrome of infantile autism indicates the importance of a genetic factor which probably concerns a cognitive deficit involving language. It also indicates the importance of biological hazards in the perinatal period which may operate either on their own or in combination with a genetic predisposition. However, uncertainty remains on both the mode of inheritance and exactly what it is which is inherited.

SUMMARY

A systematic study was made of a representative group of 21 same-sexed twin pairs (11 MZ and 10 DZ) in which at least one twin showed the syndrome of infantile autism. There was a 36 per cent pair-wise concordance rate for autism in MZ pairs compared with 0 per cent concordance in DZ pairs. The concordance for cognitive abnormalities was 82 per cent in MZ pairs and 10 per cent in DZ pairs. It was concluded that there were important hereditary influences concerning a cognitive deficit which included but was not restricted to autism. In 12 out of 17 pairs discordant for autism, the presence of autism was associated with a biological hazard liable to cause brain damage. It was concluded that brain injury in the infancy period may lead to autism on its own or in combination with a genetic predisposition. Uncertainty remains on both the mode of inheritance and exactly what is inherited.

Acknowledgements—We are deeply indebted to the many colleagues whose help made this study possible.

14697610, 1977, 4, Downloaded from https://acamh.onlinelibrary.wiley.com/doi/10.1111/j.1469-7610.1977.tb00443.x by Universite Toulouse I Capitole, Wiley Online Library on [15/04/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

We are particularly grateful to those who gave us access to their patients and who provided information about them: Mrs. L. Arendt, Dr. A. Bentovim, Dr. I. Berg, Dr. F. Bernard, Mrs. W. Brown, Dr. M. Crawford, Dr. M. Davies, Mr. C. Dyer, Dr. K. Fraser, Dr. E. Frommer, Professor P. Graham, Dr. J. Lisle, Dr. L. Minski, Dr. G. O'Gorman, Dr. M. Shepherd, Dr. G. Simon, Dr. F. Tomlinson, Dr. J. Towler, Miss D. Trowell, Dr. J. Varley and Dr. T. Weihs. Dr. J. Shields gave invaluable help in providing access to the Maudsley Hospital Twin Register, in advising us throughout the study, and in giving comments on an earlier draft of this paper. We are grateful to Professor C. Carter for allowing us access to the Hospital for Sick Children's Twin Register and for providing information on some cases; to Dr. R. Sanger who kindly undertook the blood grouping analysis for us and to Mr. Gregory Carey who undertook some of the dermatoglyphic analysis. We are also especially grateful to Dr. L. Bartak, Mrs. R. Hemsley and Mrs. P. Howlin who undertook psychological testing with a number of the twins and to Mrs. Monica White for searching the records of the National Society for Autistic Children to identify twins.

The study was supported in part by a grant from the MRC.

APPENDIX: CASE SUMMARIES OF CASES

MONOZYGOTIC PAIRS

Case 1

Zygosity determined bld. grps. Pair concordant for (atypical) autism. Male. Age 22 yr.

Family. Fa. is industrial engineer. Mo. had one episode untrtd. depression. Three older sibs: two had single episodes of severe depression.

Pregn. Hyperemesis and fainting throughout. Gestation 36 weeks.

1*st born twin.* B. wt. 5 lb 2 oz. Normal neonatal course. Normal motor milestones. Severe eczema 4–9 months so that cd. not be picked up. Lack of responsiveness noted from 9 months. Lack of eye to eye gaze. Rejected comfort and cuddling. Lack of sympathy. No friendships. No babble, speech or gesture. Food fads and pica when younger. Strong attachment to skittle up to 12 yr. Occ. repetitive brick play. No imaginative play. Finger-flicking mannerism and stereotyped gait. Head banging and wrist biting. Fits since 12 yr. Special school to 14 yr and the mental subn. hosp. EEG non-specific abn. Poor coordination, awkward gait. Language age < 1 yr. Social age 3 yr 7 months. Biochem. normal.

2*nd born twin.* B. wt. 5 lb 6 oz. Normal neonatal course. Normal motor milestones. Severe excema 4–9 months. Lack of responsiveness from 9 months. Lack of eye to eye gaze. Minimal parental attachment. No friendships. Rejected comfort and cuddling. Normal babble but no speech or gesture. V. severe food fads. Upset by changes. Puts objects into rows. No imag. play. Finger-flicking mannerisms. Carried string and waved in front of eyes up to 12 yr. Wrist biting. Fits since 16 yr. Special school to 14 yr and then mental subn. hosp. EEG non-specific abn. Fair coordination, normal gait. Language age < 1 yr. Social age 3 yr 7 months. Biochem. normal.

Case 2

Zygosity determined bld. grps. Pair concordant for autism. Male. Age 12 yr.

Family. Fa. is plumber (born W. Indies), was late talking. Mo. anxious and recurrently depressed (untrtd.). Two sibs. (one older, one younger), one behav. diffs. at school.

Pregn. Anaemia, transfusion. Gestation 40 weeks.

1*st born twin.* B. wt. 6 lb 11 oz. Normal neonatal course. Normal motor milestones. Lack of responsiveness from 1 yr. Lack of eye to eye gaze, lack of attachments, avoids contact, no friendships. Single words 8 yr; phrases 10 yr. Echolalic, pronominal reversal, stereotyped sp. Poor articulation, lack of cadence and irregular rhythm. No gesture. Hands over ears. Fixed routines re walks and meals. Repetitive stereotyped drawings. Finger-flicking mannerisms, head banging. Attends special school. Myopia, poor gross motor coordination. EEG non-specific abn. WISC FS 56. VS 50. PS 75. S.Q. 44 Peabody L.Q. 33. Reynell language comprehension age 7 yr 10 mo. (At C.A. 12·1 yr). Neale Reading Age Acc 8 yr 4 months. Comprehension No score. Biochem. normal.

2*nd born twin.* B. wt. 6 lb 13 oz. Normal neonatal course. Normal motor milestones. Lack of responsiveness from 2nd yr. Lack of differentiation people to 5 yr. Minimal parental attachment.

14697610, 1977, 4, Downloaded from https://acamh.onlinelibrary.wiley.com/doi/10.1111/j.1469-7610.1977.tb00443.x by Universite Toulouse 1 Capitole, Wiley Online Library on [15/04/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Solitary play, no friendships. No babble in 1st 2 yr. Single words 2 yr, phrases 5 yr. Echolalia, stereotyped phrases, little social speech, lack of cadence up to last 2 yr. Head banging and pica when younger. Finger-flicking mannerisms. Strong attachment to toy soldiers (takes to bed). Repetitive, stereotyped play and drawing. Upset by changes routine. Bath ritual. Marked improvment after age 10 yr so that now friendly with adults and using normal speech appropriately. Lack of friendships remain. Attends special school. Myopia, strabismus, poor coordination. EEG non-specific abn. Biochem. normal. WISC FS 57. VS 60. PS 57. S.Q. 59, Peabody, L.Q. 57. Neale Reading Age (when C.A. 12·1 yr). Acc. 9 yr. 1 month. Comprehension 7 yr 3 months.

Case 3

Zygosity determined bld. grps. Pair concordant for (atypical) autism. Male. Age 14 yr.

Family. Fa. is porter, Mo. nurse. Four older sisters.

Pregn. normal, 34 weeks, gestation. 24 hr labour.

1*st born twin.* Breech. B. wt. 5 lb 10 oz. Normal neonatal course. Normal motor milestones. Severe crying and sleep dist. in infancy. Not cuddly, did not come for comfort, lack of differentiation people to 5 yr. Normal smiling and eye to eye gaze. No group play of friendships. Odd words only, occ. echoing. Upset by noise. No gesture. Whirls self and spins knives. Likes shiny objects. Various food fads. Pica (total lead intoxication). Wrist biting. Destructive. Restless. Special school to 11 yr and then mental subn. hosp. EEG sharp wave focus. Strabismus, wide-based gait, poor motor coordination. Mecham language age < 1 yr. Social age 18 months.

2*nd born twin.* Breech. B. wt 5 lb 4 oz. Normal neonatal course. Normal motor milestones. Severe crying and sleep dist. in infancy. Not cuddly, lack of differentiation people to 5 yr. Normal smiling and eye to eye gaze. No group play or friendship. Odd words only, occ. echoing. V. upset by noise, puts fingers in ears. No gesture. Age 3–5 yr severe screaming, aggression, and destruction. Breaks windows and furniture. Upset by changes. Attracted shiny objects. Likes to be swung around, likes spinning knives. Food fads. V. severe pica (total lead intoxication). Severe head banging, face slapping, pulled out hair. Occ. hand mannerisms. Toe walking when younger. Special school to 11 yr and then mental subn. hosp. One recent (major) fit with some social deterioration. EEG sharp wave focus. Strabismus. Poor coordination and wide-based gait. Planter responses equivocal. Mecham language < 1 yr. Social age 18 months.

Case 4

Zygosity determined bld. grps. Pair concordant for autism (one atypical). Male. Age 8 yr.

Family. Fa. univ. teacher. Mo. had one previous pregn.—terminated because hydramnios. Bilingual family.

Pregn. Vomiting early months. Pre-eclamptic toxaemia. Induced 39 weeks.

1*st born twin.* B. wt. 6 lb. 10 oz. Low forceps. Normal neonatal course. Normal motor milestones. Normal development apart from pronominal reversal until 3 yr when became anxious, tearful, upset. Speech deteriorated to poorly articulated monosyllables. After 6 months gradual improvement. Normal eye to eye gaze and normal relationship parents. Does not play peers and regarded as odd by them. Speech complex but stereotyped and echolalic: pronominal reversal, little appreciation of abstract. Upset by changes. Attached to cardboard buses which he carries around. Repetitive drawing buses and copying newspaper adverts. Limited imagination. Attends normal school. Leiter I.Q. 90, S.Q. 89. Mecham L.Q. 113.

2*nd born twin.* B. wt. 5 lb. Born 30 min after twin, foetal distress and uterine inertia. Given positive pressure O^2, breathed 7 min. Urinary tract infection. Disch. hosp. after 4 weeks. Diffs. feeding. Lack of cuddling. Normal motor milestones. Absorbed twiddling cotton reel at 8 months. Blank facial expression and lack of eye to eye gaze. Not attached to parents until after 2 yr and then limited. No friendships, some beginning of limited grp. play. Normal babble. First words 58 months—still few words only, occ. echolalia. Waves bye-bye. Excellent memory spatial relationships. Dislikes new situations. Several attachments to odd objects (e.g. buttons), swings string in front of face. Hand twisting mannerism and odd gait. Repetit. stereotyped play. Pica. Attends special school. Biochem. normal. M.P. I.Q. 51. S.Q. 32. Mecham language age < 18 months.

Case 5

Zygosity determined bld. grps. Pair discordant for autism, concordant for cognitive and social/emotional disorder. Female. Age 15 yr.

14697610, 1977, 4, Downloaded from https://acamh.onlinelibrary.wiley.com/doi/10.1111/j.1469-7610.1977.tb00433.x by Universite Toulouse 1 Capitole, Wiley Online Library on [15/04/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Family. Fa. engineer (univ. grad.). One normal older sister. Mo. also had one still birth at 7 months.

Pregn. Bleeding at 2 months. 39 week gestation. Twins not diagn. and delivery at home.

1*st born twin.* B. wt. 5 lb 8 oz. Normal neonatal course. Sat 10 months. Walked 21 months. Normally cuddly responsive baby. Single words 20 months. Phrases 36 months. Normal usage speech. Became more passive when tormented by autistic sib. twin. Shy sensitive girl with low self-esteem but otherwise normal social relationships—affectionate, sympathetic and has a few friends. Behav. normal. Normal school until 11 yr and then special school (ESN). WISC I.Q. FS 51. VS 61. PS 48. Reading age 8 yr 10 months. S.Q. 115. Poor coordination.

2*nd born twin.* B. wt. 5 lb. Breech. Delay in breathing. Cord v. narrow and white. Haemorrhagic disease 2 days. Sat 10 months. Walked 23 months. Lack of responsiveness from infancy: not interested in people, distressed by noise, wd. crawl on wood but not carpet. No attachment to parents until after 5 yr and then minimal. Lack of eye to eye gaze, did not come for comfort. Approaches small children but no play with peers and no friendships. Some echoed words at 30 months but no phrases until 6 yr. Speech still stereotyped and repetitive with much delayed echoing. Marked resistance to all changes. Rigid stereotyped play with multiple routines and rituals. Various attachment to odd objects. Facial grimaces, hand flapping and mannerism, bouncing gait. Pica in early childhood. Head banging and wrist biting age 3–6 yr. Strabismus. Clumsy. Awkward gait. Merrill–Palmer I.Q. 28. S.Q. 40. Mecham I.Q. 29.

Case 6

Zygosity determined bld. grps. Pair discordant for autism, concordant for cognitive and social/emotional disorder. Male. Age 10 yr.

Family. Fa. tradesman. One normal older sister. Mo. also had one still birth.

Pregn. Severe vomiting first trimester. Toxaemia last trimester; 2 admissions. 39 week gestation.

1*st born twin.* B. wt. 6 lb 7 oz. Normal neonatal course. Normal motor milestones. Severe excema in first year—mild since with occ. asthma. Responsive but difficult baby, often crying, v. poor sleeper. Did not come for comfort. Variable eye to eye gaze. Often rocks and appears detached. No group play, no friendships, some parallel play with twin. Some echoed words at 2 yr but diminished at $2\frac{1}{2}$ yr. Now only echolalia and some spont. single words. No social usage sp. Slow to adapt to new situations. Lines up objects in rows. Good with constructional toys but no representational or imaginative play. Prefers routines. Severe dog phobia. Finger flicking mannerisms, rocks, grimaces. Pica. Head banging up to 5 yr. Attends special school. Pleasant temperament now but v. little reciprocity in social interaction. WISC Non-verbal I.Q. 83. S.Q. 34. Mecham language age 18 months.

2*nd born twin.* B. wt. 6 lb 4 oz. Normal neonatal course. Normal motor milestones. Excema and asthma for 4 months. Phrase speech before 2 yr. Now uses language normally but mild articulation defect. Sociable and friendly but rather immature and had severe dog phobia until a year ago. Behav. normal. Creative, imaginative play. Has won friends. Attends special school (ESN). WISC VS 79. PS 100. S.Q. 97. Mecham L.Q. 89. Poor fine motor coordination. Motor overflow.

Case 7

Zygosity determined bld. grps. Pair discordant for (atypical) autism, concordant for cognitive and social/emotional disorder. Female. Age 12 yr.

Family. Fa. Business manager. One normal older brother.

Pregn. Bleeding at 3 and 4 months. 35 week gestation.

1*st born twin.* B. wt. 4 lb. In hosp. 21 days for slow wt. gain. Normal neonatal course. Normal motor milestones. Cuddly responsive baby. Single words by 1 yr and phrases before 2 yr. Marked articulation defect to 7 yr. Talkative, sociable girl with many friends. V. sympathetic and emotionally concerned—befriends children with diffs. V. sensitive worrier; cries daily with imagined slights and failures at school. Apprehensive of new situations. Reluctance to attend school (ordinary). Merrill–Palmer I.Q. above av. S.Q. 104. Mecham L.Q. 122.

2*nd born twin.* Breech. B. wt. 5 lb 4 oz. In hosp. 14 days. Normal neonatal course. Normal motor milestones. Single words 2 yr. Normal develop. apart from immature speech and poor articulation until $4\frac{1}{2}$ yr when had severe febrile illness and profound change in behav. Lost social responsiveness, marked reduction in speech, eating poor, appeared aimless, ceased to play. Until 6 yr lack of personal

14697610, 1977, 4, Downloaded from https://acamh.onlinelibrary.wiley.com/doi/10.1111/j.1469-7610.1977.tb00433.x by Universite Toulouse 1 Capitole, Wiley Online Library on [15/04/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

interaction, blank expression, lack of eye to eye gaze. Now somewhat more responsive but no friends. Stereotyped phrases, monotone, no social speech, echoes, poor articulation, excellent word memory. Eating rituals, repetitive drawing, rocking. No imag. play. Helps in house. Awkward gait. Attends special school. Merrill–Palmer I.Q. (non verbal) 98. S.Q. 41. Mecham I.Q. 29.

Case 8

Zygosity determined dermatoglyphics and appearance. Pair discordant for autism, concordant for cognitive and social/emotional disorder. Male. Age 10 yr.

Family. Fa. business manager. One younger sister (4 yr) with echoing and poor articulation. Lines up objects. Normal social relationships and normal social usage language. Having psychiat. trt. for encopresis. There are several eccentrics in mo.'s family.

Pregn. Bleeding at 3 months. Hydramnios. 35 week gestation. Both twins born with forceps for uterine inertia.

1st born twin. Face presentation. B. wt. 4 lb 11 oz. Normal Apgar score. In hosp. 50 days because of feeding diffs. from cleft palate. I.P. 1 wk pneumonia at 4 months. Several operations for congenital anomalies. Sat 9 months, walked 22 months. Not bowel trained until 9 yr. Lack of social smiling and responsiveness in first year. Stared at sun, refused to eat at 2 yr. Blank expression and lack of eye to eye gaze. No response to parents before 5 yr. No play with children. Echolalic speech 3 yr but no meaningful words until 6 yr. Now single words and stereotyped phrases. No social use sp. Marked resistance to change of routine or furniture. Carries string and flicks it. Various fixed routines. Likes to touch shiny objects. Used to rock and clap hands. No appropriate play. Severe pica. Attends special school. Rt. ptosis, fixed pupil and external palsy. Left strabismus and nystagmus. Repaired hare lip. Poor coordination. Merrill–Palmer I.Q. 24. S.Q. 17. Mecham L.Q. 18.

2nd born twin. Vertex. B. wt. 4 lb 12 oz. Normal Apgar score. In hospital 17 days. Normal neonatal course. Normal motor milestones. Cuddly, responsive baby. Single words 24 months, phrases after 3 yr. Stutters when excited, v. poor articulation. Vocab. adeq. but limited social speech. Normal relationships parents. Only recently started to play peers; does not initiate interaction. Anxious. No resistance to change. Series of circumscribed solitary interests (currently marbles). Also imag. play. Clumsy and socially gauche. Attends normal school but had special tutoring in reading and spelling. Slow fine motor movements. Shy but friendly boy. WISC VS 108. PS 122. S.Q. 95. Mecham L.Q. 70. Diagnosed as ? autistic psychopathy.

Case 9

Zygosity determined bld. grps. Pair discordant for autism, concordant for cognitive disorder. Female. Age 5 yr.

Family. Fa. street trader. Mo. I.P. 9 months for depression following misc. Nine older sibs and one younger. Mo. also had three misc.

Pregn. 34 wk gestation.

1st born twin. B. wt. 3 lb 6 oz. Normal neonatal course. In hosp. 3 weeks. Sat 13 months. Walked 21 months. Single words 2 yr, phrases soon after. Still wet at night. Not as cuddly or responsive as sibs in infancy. Normal relationship with parents but slightly less sympathetic and affectionate than sibs. Plays well with sibs but less with peers at school. Imag. play. Drawing immature. Normal usage of speech but articulation imperfect. Attends normal school. At interview appears friendly, responsive, inquisitive girl. Asymmetrical ears. S.Q. 70. Mecham L.Q. 82.

2nd born twin. B. wt. 4 lb 15 oz. Slow wt. gain. In hospital 1 month. Sat 15 months. Walked 24 months. Still wets and soils. During 1st year blank expression, wd. not be cuddled or consoled, sensitive to noise and did not respond to voice. Lack of eye to eye gaze, no parental attachment, no play with peers. In last year, became more responsive and cuddly. Some parallel play sibs. No speech; beginnings of babble. Likes set routines, will drink only from red cups. Routines. Twiddles things in front of her eyes. Finger twisting mannerisms and rocking. No imag. play. Attends special school. Right strabismus. D.Q. 40. S.Q. 32. Mecham language age < 1 yr.

Case 10

Zygosity determined bld. grps. Discordant pair (atypical autism). Male. 7 yr.

Family. Fa. accountant: late in speaking, said little before starting school. Odd personality. Mo.

14697610, 1977, 4, Downloaded from https://acamh.onlinelibrary.wiley.com/doi/10.1111/j.1469-7610.1977.tb00443.x by Universite Toulouse I Capitole, Wiley Online Library on [15/04/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

trtd. as I.P. for depression. Older bro. did not speak until 2½ yr. Socially awkward and no friends until 6 yr. Interested in maps and routes. Mo. also had one misc.

Pregn. Normal. 39 week gestation.

1st born twin. B. wt. 6 lb. Normal neonatal course. Normal motor milestones. Single words 18 months. Phrases 2 yr. Happy sociable infant. At 3 yr deterioration in speech, lack of emotional response, screaming, lack of response to sounds. Now blank facial expression, limited eye to eye gaze, no sympathy, no play with sibs or peers. Attached to mother. Stereotyped repetitive speech, echoing, monotone. Dislikes changes. Draws repetit. patterns. Puts toys in rows. Used to carry around odd objects (e.g. piece of linoleum). Strictly followed routines. Food fads. Hand and finger mannerisms. Rocks. Attends special school. Normal neurol. Merrill–Palmer I.Q. 68. S.Q. 44. Mecham L.Q. 37.

2nd born twin. B. wt. 5½ lb. Tube fed 24 hr because would not suck but otherwise normal neonatal course. Normal motor milestones. Not a partic. cuddly baby but normally responsive and developed appropriate parental attachment. Sociable and enjoys his friendships. Good creative play. Single words 18 months. Phrases 20 months. Normal level and usage of language. Behav. normal. Attends normal school. Merrill–Palmer I.Q. 100. S.Q. 107. Mecham L.Q. 117.

Case 11

Zygosity determined by dermatoglypics. Discordant pair. Male 9 yr.

Family. Fa. business manager. Three older and one younger normal sibs. Parents divorced.

Pregn. 34 week gestation. Mo. ill in bed most of pregnancy.

1st born twin. B. wt. 5 lb. Tube fed several days. In incubator 1 week and left hospital 4 weeks after birth. Normal milestones. Phrase speech before 2 yr. Shy child in pre-school yrs. Now plenty of friends. No social, emotional or behav. problems. Apprehensive re dentist and medical attention. Attends normal school. WISC I.Q. FS 107. VS 109. PS 103. Normal language.

2nd born twin. B. wt. 4 lb 1 oz. One neonatal convulsion. In incubator 1 week. Thrived poorly and persistent feeding difficulties. Left hosp. 6 weeks after birth but readmitted twice during next 18 months. Unresponsive difficult baby, did not smile and did not want to be held. Lack of eye to eye gaze. Mother very distressed by difficulties and after a while could not bear to deal with child; no relationship with parents until after 6 yr. Lack of sympathy. Now beginning to play with peers. Good fine motor coordination but did not walk until 2½ yr. Lack of babble. Single words after 2 yr; phrase speech 3 yr 10 months. Early echolalia and stereotyped phrases. Little social speech; poor abstraction and conceptualization. Counting rituals when younger. Follows routines. Repetitive stereotyped drawings. In psychiat hosp. age 2–5 yr. Since lived with father. Now attends normal school. I.Q. Biret 100. S.Q. 80. Mecham L.Q. 81. Manneristic gait; otherwise neurol. N.A.D.

DIZYGOTIC PAIRS

Case 12

Zygosity on bld. grps. Pair discordant for autism, concordant for cognitive disorder. Male. 5 yr.

Family. Fa. accountant; rather obsessive personality, no social life. Two paternal uncles with definite social oddities; without friends, unusual circumscribed interests, unmarried, fastidious and precise. Normal older sister. Older bro. now normal but ? late in onset of speech, also head banging and resistance to change as baby.

Pregn. High B.P. Mo. I.P. × 3 for rest. 39 week gestation. Mo. is Rh neg. but no antibodies.

1st born twin. B. wt. 5 lb 12 oz. Dysmature appearance. Bilirubin rose to 10 mg. In special care unit. Lowest bld. sugar was 36 mg %. Motor milestones delayed. Walked 23 months. Lack of responsiveness and social smile in 1st yr. Does not want to be held or picked up. Variable eye to eye gaze. No interaction children. Sensitive to noise. Abn. babble. Single words 3 yr. Echolalia. Lack of social speech. Slow to adapt to new situations. Food fads. Various fixed routines (walks, meals, bedtimes). Puts toys in rows. No imag. play. Attends special school. Hand-flapping mannerism. Stiff-legged gait. Alternating strabismus. Poor gross motor coordination (fine O.K.). Merrill–Palmer I.Q. (non-verbal) 67. S.Q. 50. Mecham L.Q. 28.

2nd born twin. Breech. B. wt. 7 lb 9 oz. Normal neonatal course. Motor milestones delayed. Walked 21 months. Cuddly responsive baby. Single words 30 months. Phrases after 3 yr. Some echolalia. Occ. stereotyped repetitive phrases but also social speech. Behav. normal. Some imag. play. Friendly, sociable boy. Attends normal school. Merrill–Palmer I.Q. 74. S.Q. 82. Mecham L.Q. 60.

14697610, 1977, 4, Downloaded from https://acamh.onlinelibrary.wiley.com/doi/10.1111/j.1469-7610.1977.tb00443.x by Universite Toulouse 1 Capitole, Wiley Online Library on [15/04/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Case 13

Zygosity on marked diffs. appearance. Pair discordant for (atypical) autism, concordant for social/emotional disorder. Male. 18 yr.

Family. Fa. commercial artist (died when twins 13 yr). Had unusual personality and circumscribed interests. No sibs. Bilingual family.

Pregn. Severe vomiting. Mo. I.P. for 2/52 at 3 months. 41 week gestation. Obstructed labour 24 hr. Caesarian section after failed forceps delivery.

1st born twin. B. wt. 6 lb 4 oz. Normal neonatal course. Normal motor milestones. Played with faeces until 3½ yr. Cuddly but less responsive than sib. Sensitive to noise. Babble diff. from twin. Speech delayed but dates not recalled. Echolalia; repetition of phrases; stereotyped stilted speech; slow, ponderous way of talking; little social sp. Early lack of attachment to parents and continued lack of interaction with peers. First parental concern when did not settle at nursery school age 4 yr. Vague expression, limited eye to eye gaze. Slow to adapt to new situations. Markedly attached to rubber toy for several yr. Draws soldiers very repetitively. Collects epaulettes which he attaches to his clothes. Numerous hand and finger mannerisms. Attended special school to 16 yr. Rocking. Fits from 9 yr (only 4 in all). Uncertain variable EEG abn. Neurol. normal. WISC VS 62. PS 75. S.Q. S.Q. 43. Mecham L.Q. 30.

2nd born twin. B. wt. 8 lb. Rectal abscess at 6 weeks. Normal neonatal course. Normal motor milestones. Normal social and emotional develop. Did well at school. Passed 'O' levels at 16 yr. At 17 yr gradually stopped attending school, kept to his room, refused to get job. Surly and unpleasant to family. Held job for short while. Accepted at several colleges but attended courses for few days only. Spends time lying in bed reading about cybernetics and listening to music. WISC I.Q. VS 108. PS 131. Normal social maturity. Normal language. No thought disorder, delusions or hallucinations.

Case 14

Zygosity determined by bld. grps. Pair discordant. Male. 17 yr. Autistic twin and his caretakers seen. Mo. interviewed by 'phone. Normal twin not seen.

Family. Fa. farm owner. Anxious man prone to depression (not trtd.). Mo. slow to talk and reading diffs. until 10 yr. Two younger sisters, both of whom had exchange transfusions; one having psychiat. trt. (no details).

Pregn. Mo. Rhesus neg. with antibodies. Mo. had high B.P. and toxaemia—I.P. for 5 weeks before delivery. Caesarian section at term.

1st born twin. B. wt. 6 lb. 9 oz. Poor condition at birth with heavy meconium staining and severe jaundice—needed resuscitation. Cord bilirubin 10·8. Three exchange transfusions. Sat 11–12 months. Walked 20–24 months. Toilet trained after 8 yr. Passive and unresponsive in first year. Lack of social smile, blank facial expression, lack of eye to eye gaze when young (now strange fixed stare), lack of attachments, ignores people. Lack of response to sounds (hearing normal). No speech. Takes hand to indicate needs. Food fads. Will not wear new clothes. Continuously flicks bits of paper in front of eyes. Attached to odd objects (boxes, bottles, bits of paper). Twists crinkly paper, jumps, pivots and leaps about room. No imag. play. Manneristic gait. In hosp. age 2 yr for 1 wk measles. Attended autistic unit for few years. In mental subn. hosp. since 9 yr. Normal EEG. Poor coordination. At age 6 yr his Merrill–Palmer I.Q. (non-verbal) was 76 but at age 14 yr his non-verbal I.Q. was only 30. S.Q. 13. Mecham language age < 1 yr.

2nd born twin. B. wt. 6 lb 15 oz. Good condition at birth. Cord bilirubin 4·2. Later had two exchange transfusions. Normal motor milestones. Phrase speech before 2½ yr. Normal relationships. No social, emotional or behav. problems. Attends normal school. Above av. attainment. Obtained six 'O' levels.

Case 15

Zygosity on basis of marked diffs. appearance. Discordant pair. Male. 16 yr.

Family. Fa. draughtsman. No sibs.

Pregn. Toxaemia. 36 week gestation.

1st born twin. B. wt. 4 lb. In incubator 10 days. In hosp. 30 days eye infection. Vomited and cried in first months. Slow feeder. Normal motor milestones. Lack of eye to eye gaze and failure to cuddle

14697610, 1977, 4, Downloaded from https://acamh.onlinelibrary.wiley.com/doi/10.1111/j.1469-7610.1977.tb00443.x by Universite Toulouse I Capitole, Wiley Online Library on [15/04/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

noted at 6 months. No parental attachment, did not come for comfort, no interaction other children. Blank or solemn facial expression. Single words 2½ yr, phrases 5 yr. Speaks little. Stereotyped phrases (echolalia when younger)—immature grammar, poor articulation. Some metaphorical lang. Sing-song voice. Puts objects in rows. Refuses to go to new places. Various odd attachments (e.g. to hammers and then to soaps—all brands known by smell). At one time wd. only eat square things. Various quasi-obsessive interests. Hand and finger mannerisms. Rocks. Shakes string back and forth. Pica. No imag. play. Special school to 9 yr and then mental subn. hosp. Strabismus. Dysmorphic appearance. Poor coordination. Abn. gait. Normal EEG. Cystinuria. Merrill–Palmer I.Q. (non-verbal) 43. S.Q. 14. Mecham language age < 2 yr.

2nd born twin. B. wt. 5 lb 8 oz. Not in incubator. Normal neonatal course. Normal motor milestones. Single words 18 months, phrases 2½ yr. Normal usage lang. Normal social, emotional and behav. dvelop. Normal, responsive, sltly. shy adolescent. Attends academically selective school and has above av. attainments. S.Q. 103. Cystinuria. Optic atrophy left eye—otherwise neurol. normal.

Case 16

Zygosity on basis of marked physical diffs. Discordant pair. Male. 22 yr.

Family. Fa. teacher. Two older and one younger sib—all normal and above av. intelligence.

Pregn. 34 week gestation. Prolonged labour.

1st born twin. B. wt. 4 lb 6 oz. Normal neonatal course. One febrile convulsion. Normal motor milestones. Fully normal development in all respects. Sociable, friendly univ. graduate. Interviewed by 'phone.

2nd born twin. B. wt. 4 lb 10 oz. Born 75 min after twin. Uterine inertia. Fed slowly. Normal motor milestones. Lack of social responsiveness after 1 yr. Detached expression. Lack of interest in people. No understanding emotion, no sympathy, still has no sense of socially appropriate. Single words 5 yr. Phrases 7½ yr. Early echoing and neologisms. Still little social speech, stereotyped lang., no understanding abstract, flat intonation, slow ponderous speech. Strict adherence to daily routines which rule family life. Always carries calendar and railway timetable. Plans journeys in excruciating detail. Draws very well but v. repetitively. Excellent spatial memory (able to make accurate models and floor plans from memory). Hand mannerisms when young, still has odd movements when excited. Attended special school. EEG non-specific abn. Air encephalogram basically normal but slight dilatation right lat. ventricle. Osteoma right arm. Biochemistry normal. WISC VS 50. PS 93. S.Q. 62. Mecham L.Q. 34.

Case 17

Zygosity on basis of marked physical diffs. Also probably diff. bld. grps. (because only one twin had erythrobtastosis foetalis). Discordant pair. Male. 13 yr.

Family. Fa. electrician (born West Indies). Three older children all normal and of above av. attainment (two passed 'O' levels and third not yet at that age). Mo. occ. depressed (not tretd.).

Pregn. Mo. Rhesus neg. with antibodies. 33 week gestation.

1st born twin. B. wt. 4 lb 2 oz. Bilirubin 19·5 mg % on day 3. Exchange transfusion. Apnoea and cyanosis day 5. Tube fed through day 7. In hosp. 33 days. Apparently normal motor milestones (dates not recalled). Would not be cuddled in early years. Blank expression. Lack of eye to eye gaze. Some attachment mother. Ignores other children. No speech. Hands over ears. No gesture. Resists changes in furniture and ornaments. Insists on same routes on walks. Mealtime ritual. Carried around bricks when younger. Compulsive touching of people's shoulders. Facial grimaces, rocks, finger-flicking mannerisms. Bites wrists and bangs head. No imag. play. In mental subn. hosp. Normal physical exam. except bilat. undescended testicles. Biochemistry normal. EEG low amplitude spikes right temporal region. Merrill–Palmer I.Q. (non-verbal) 43. S.Q. 36. Mecham language age < 1 yr.

2nd born twin. B. wt. 3 lb 7 oz. Born 1 hr after twin. Forty days in hospital for wt. gain but not jaundiced or transfused. Normal motor milestones. Well behaved social, friendly child without problems. Av. attainments at ordinary school. Excels in sports but poor fine motor coordination. S.Q. 90. Mecham L.Q. 80.

Case 18

Zygosity determined bld. grps. Discordant pair. Female, 12 yr.

14697610, 1977, 4, Downloaded from https://acamh.onlinelibrary.wiley.com/doi/10.1111/j.1469-7610.1977.tb00443.x by Universite Toulouse 1 Capitole, Wiley Online Library on [15/04/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Family. Fa. factory foreman. Two older bros. both psychiat. normal but one had tutoring for reading diffs.

Pregn. Normal 40 week gestation.

1*st born twin.* B. wt. 5 lb 13 oz. Vertex. Sucked poorly and fed slowly, otherwise normal neonatal course. Sat 10–11 months. Walked 30 months. Socially unresponsive infant. Screaming, rocking and inattention at 12 months. No smiling until 6–7 months. Not cuddly. Lack of eye to eye gaze, blank expression. Lack of parental attachment, never came for comfort. No interaction peers. Little babble, no speech, no gesture. Very upset by any changes. Puts objects in piles. Insists on set routines. Attachment to kitchen spoon 1–4 yr. Dextrous at spinning plates. Swings string in front of face. Constant hand and finger mannerisms, rocking. No imag. play. Pica when younger. Age 4 yr stuck object up rectum causing peritonitis. Infectious hepatitus age 12 yr when develop. fits. In mental subn. hosp. Left strabismus. Good fine but poor gross motor coordination, awkward gait. Hypotonia. Normal EEG. Biochemistry normal. S.Q. 23. Mecham language age < 1 yr.

2*nd born twin.* B. wt. 6 lb 10 oz. Normal neonatal course. Normal motor milestones. Normal social, emotional and behav. develop. Interesting, enthusiastic and talkative adolescent. Attends ordinary school and attainments above average. S.Q. 111. Normal language.

Case 19

Zygosity on basis marked physical diffs. Pair discordant (atypical autism). Female. Age 14 yr.

Family. Fa. printer. Died when twins 10 yr. Two older bros.; one autistic and mentally retarded (not seen but no speech, lack of eye to eye contact, hand and finger mannerisms and attachment to unusual objects). Strong F.H. on father's side of severe myopia.

Pregn. Severe vomiting first trimester. 40 week gestation.

1*st born twin.* B. wt. 5 lb 9 oz. Vertex. Normal neonatal course. Normal motor milestones. Phrases by 12 months. Normal social, emotional and behav. develop. (although verbally precocious). Friendly, sociable, attractive adolescent. Attends ordinary school and is top of class. Gross myopia from early age. Severe bilat. uveitis age 7 yr requiring extensive hospitalization and trt. with steroids. Apart from eyes, normal on examination. S.Q. 125. Normal language.

2*nd born twin.* B. wt. 6 lb 6 oz. Born 45 min after twin. Delay in crying but otherwise normal neonatal course. Sat 9 months. Walked 26 months. Lack of eye to eye gaze, blank expression, gazed at hands in 1st yr. Came for comfort and fond of parents but detached and did not give affection. Approaches and joins in with other children but no friendships. No social sense, asks embarrassing Q of strangers. Very sensitive to noise but lack of response to voice when young. Single words 2 yr, phrases 4 yr. Early echolalia, pronominal reversal to 13 yr, stereotyped phrases, monotone, little social speech. Many rituals revolving around time. Repetitive stereotyped play. Attached to partic. hat for yrs. Collects bottles. Limited imag. play. Rocks. Attends special school. Left strabismus. Abn. right optic disc. Severe myopia. Poor coordination, choreiform movements. Non-verbal I.Q. 59. S.Q. 49. Mecham I.Q. 49.

Case 20

Zygosity on basis marked physical diffs. Pair discordant. Male. 6 yr.

Family. Fa. artist. Mo. had psychiat. trt. for emotional dist. One normal younger sib.

Pregn. Normal. 36 week gestation.

1*st born twin.* B. wt. 5 lb 15 oz. Normal neonatal course. Normal motor milestones. Normal social, emotional and behav. develop. Attends normal school. Serious, creative, talented and imag. child. WISC FS 142. VS 154. PS 121. S.Q. 102. Mecham I.Q. 122.

2*nd born twin.* Breech. B. wt. 5 lb 5 oz. Resuscitated. Apnoea 9 min. Poor sucking. Normal motor milestones. No social smile until after 9 months. Lack of cuddle, interest, response, and eye to eye gaze in first yr. Lack of parental attachment until 3 yr but now relates well to family and beginning to play with peers. Slightly socially disinhibited and asks personal questions of strangers. Impulsive. V. sensitive to noise. Speech began at 3 yr; at first stereotyped and repetitive but normal level of usage in last yr. Marked distress with new situations when younger but not now. Likes routines. Finger mannerisms when younger. Repetitive play and lack of imagination until last yr—now normal. Attends normal school. Left strabismus. Notched left earlobe. Poor fine motor coordination. Air encephelogram showed left cortical atrophy. EEG focal abn. on left. WISC FS 115. VS 125. PS 100. S.Q. 81. Mecham L.Q. 104.

14697610, 1977, 4, Downloaded from https://acamh.onlinelibrary.wiley.com/doi/10.1111/j.1469-7610.1977.tb00433.x by Universite Toulouse 1 Capitole, Wiley Online Library on [15/04/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Case 21

Zygosity on basis diffs. in appearance. Pair discordant. Female. 20 yr. Extensive info. from case notes and other reports but family not seen.

Family. Fa. salesman with recurrent manic–depressive illness.

Pregn. Severe vomiting first trimester. 34 week gestation.

1*st born twin.* B. wt. 5 lb 6 oz. Normal neonatal course. Shy and anxious at time of Fa.'s illness but otherwise a friendly sociable girl with many friends. No behaviour diffs. Above av. attainment. Currently a univ. student.

2*nd born twin.* Breech. B. wt. 4 lb 13 oz. Born 30 min after twin. Slow feeder. Kept in hosp. 5 weeks. Normal motor milestones but enuretic to age 8 yr. Cried freq. Unaffectionate, unresponsive baby. Lack of eye to eye gaze, little interest in people, superficial relationships. Little interaction other children, no friendships. Late onset babble. Single words 36 months, phrases 10 yr. Persistent echolalia, pronominal reversal, stereotyped repetitions of phrases, poor articulation. Repetitive representational drawing. No imag. play. Tantrums on change of routine. Various compulsive activities. Early attachment to odd objects. Hand flapping. Bites arm. Drinks large quantities. Attended special school and then sheltered workshop. Normal EEG and air encephalogram. Hypotonia, high arched palate—otherwise neurol. normal. Biochemistry normal. WISC FS 45. VS 48. PS 50. Peabody I.Q. 55.

REFERENCES

BAKWIN, H. (1954) Early infantile autism. *J. Pediat.* **45,** 492–497.

BARTAK, L., RUTTER, M. and COX, A. (1975) A comparative study of infantile autism and specific developmental receptive language disorder. I. The children. *Br. J. Psychiat.* **126,** 127–145.

BARTAK, L., RUTTER, M. and COX, A. (1977) A comparative study of infantile autism and specific developmental receptive language disorders—III. Discriminant functions analysis. *J. Autism Childhood Schizophrenia* (in press).

BÖÖK, J. A., NICHTERN, S. and GRUENBERG, E. (1963) Cytogenetical investigations in childhood schizophrenia. *Acta psychiat. scand.* **39,** 309–323.

BRASK, B. H. (1967) The need for hospital beds for psychiatric children: an analysis based on a prevalence investigation in the County of Århus. *Ugeskr. Laeg.* **129,** 1559–1570.

BROWN, J. L. (1963) Follow-up of children with atypical development (infantile psychosis). *Am. J. Orthopsychiat.* **33,** 855–861.

BRUCH, H. (1959) Studies in schizophrenia. *Acta psychiat. neurol. scand.* Suppl. 130.

CHAPMAN, A. H. (1957) Early infantile autism in identical twins. *A.M.A. Archs Neurol. Psychiat.* **78,** 621–623.

CHAPMAN, A. H. (1960) Early infantile autism. *A.M.A. J. Dis. Child.* **99,** 783–786.

CHESS, S., KORN, S. J. and FERNANDEZ, P. B. (1971) *Psychiatric Disorders of Children with Congenital Rubella.* Brunner/Mazel, New York.

CLINE, D. W. (1972) Videotape documentation of behavioural change in children. *Am. J. Orthopsychiat.* **42,** 40–47.

CREAK, M. and INI, S. (1960) Families of psychotic children. *J. Child Psychol. Psychiat.* **1,** 156–175.

CURNOW, R. N. and SMITH, C. (1975) Multifactorial models for familial diseases in man. *J. R. statist. Soc. Am.* **138,** (2), 131–169.

DOLL, E. A. (1947) *Vineland Social Maturity Scale.* Educational Test Bureau, Minneapolis.

DRAGE, J. S. and BERENDES, H. (1966) Apgar scores and outcome of the new born. *Pediat. Clin. N. Am.* **13,** 637–643.

DUNN, P. M. (1965) Some perinatal observations in twins. *Dev. Med. Child Neurol.* **7,** 121–134.

GEDDA, L. (1961) Twins. *History and Science.* C. C. Thomas, Springfield, IL.

GERVER, J. M. and DAY, R. (1950) Intelligence quotient of children who have recovered erythoblastosis fetalis. *J. Pediat.* **36,** 342–348.

GITTELSOHN, A. M. and MILHAM, S. (1965) Observations on twinning in New York State. *Br. J. prev. soc. Med.* **19,** 8–17.

GOTTESMAN, I. I. and SHIELDS, J. (1976) A critical review of recent adoption, twin, and family studies of school and family studies of schizophrenia: behavioural genetic perspectives. *Schizophrenia Bull.* **2,** 360–401.

1469/7610.1977.4 Downloaded from https://acamh.onlinelibrary.wiley.com/doi/10.1111/j.1469-7610.1977.tb00443.x by Université Toulouse I Capitole, Wiley Online Library on [15/04/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

HANSON, D. R. and GOTTESMAN, I. I. (1976) The genetics, if any, of infantile autism and childhood schizophrenia. *J. Autism Childhood Schizophrenia* **6,** 209–234.

HAVELKOVA, M. (1967) Abnormalities in siblings of schizophrenic children. *Can. psychiat. Ass. J.* **12,** 363–369.

HINTON, G. G. (1963) Childhood psychosis or mental retardation: a diagnostic dilemma—II. Pediatric and neurological aspects. *Can. med. Ass. J.* **89,** 1020–1024.

HOLT, S. (1961) The inheritance of dermal ridge patterns. In *Recent Advances in Genetics* (Edited by PENROSE, L.), pp. 101–119. Little Brown, Boston.

HUNTER, J. A. (1968) Perinatal events and permanent neurological sequelae. *N.Z. med. J.* **68,** 108–113.

KALLMANN, F. J., BARRERA, S. E. and METZGER, H. (1940) The association of hereditary microphthalmia with mental deficiency. *Am. J. ment. Defic.* **45,** 25–36.

KAMP, L. N. J. (1964) Autistic syndrome in one of a pair of monozygotic twins. *Folia psychiat. neurol. neurochir. Neerlt.* **67,** 143–147.

KANNER, L. (1943) Autistic disturbances of affective contact. *Nerv. Child* **2,** 217–250.

KANNER, L. and EISENBERG (1955) Notes on the follow-up studies of autistic children. In *Psychopathology of Childhood* (Edited by HOCH, P. H. and ZUBIN, J.). Grune & Stratton, New York.

KEAN, J. M. (1975) The development of social skills in autistic twins. *N.Z. med. J.* **81,** 204–207.

KEELER, W. R. (1957) Stress, experimental psychology, child psychiatry. Discussion of paper presented by Leo Kanner. *APA Psychiatry Rep.* **7,** 66–76.

KEELER, W. R. (1958) Autistic patterns and defective communication in blind children with retrolental fibroplasia. In *Psychopathology of Communication* (Edited by HOCH, P. H. and ZUBIN, S.), pp. 64–83. Grune & Stratton, New York.

KEELER, W. R. (1960) Personal communication. Cited by RIMLAND (1964).

KNOBLOCH, H. and PASAMANICK, B. (eds.) (1974) *Gesell and Amatruda's Developmental Diagnosis,* third edition. Harper & Row, Hagerstown.

KOTSOPOULOS, S. (1976) Infantile autism in DZ twins: a case report. *J. Autism Childhood Schizophrenia* **6,** 133–138.

KURTZ, G. R., KEATING, W. J. and LOFTUS, J. B. (1955) Twin pregnancy and delivery. Analysis of 500 twin pregnancies. *Obstet. Gynec.* **6,** 370–378.

LEHMAN, E., HABER, K. and LESSER, S. R. (1957) The use of reserpine in autistic children. *J. nerv. ment. Dis.* **125,** 351–356.

LOTTER, V. (1966) Epidemiology of autistic conditions in young children—I. Prevalence. *Social Psychiat.* **1,** 124–137.

LOTTER, V. (1967) Epidemiology of autistic conditions in young children—II. Some characteristics of the parents and children. *Social Psychiat.* **1,** 163–173.

LOVAAS, O. O., SCHAEFFER, B. and SIMMONS, J. Q. (1965) Building social behaviour in autistic children by use of electric shock. *J. exp. Res. Personality* **1,** 99–109.

MCQUAID, P. E. (1975) Infantile autism in twins. *Br. J. Psychiat.* **127,** 530–534.

MECHAM, M. J. (1958) *Verbal Language Development Scale.* Western Psychological Services, California.

MITTLER, P. (1971) *The Study of Twins.* Penguin, Harmondsworth.

MOORE, M. (1972) A study of the aetiology of autism from a study of birth and family characteristics. *J. Irish med. Ass.* **65,** 114–120.

O'GORMAN, G. (1970) *The Nature of Childhood Autism,* 2nd edition. Butterworths, London.

ORNITZ, E. M. (1973) Childhood autism: a review of the clinical and experimental literature. *Calif. Med.* **118,** 21–47.

ORNITZ, E. M., RITVO, E. R. and WALTER, R. D. (1965) Dreaming sleep in autistic twins. *Archs gen. Psychiat.* **12,** 73–79.

POLAN, C. G. and SPENCER, B. L. (1959) A checklist of symptoms of autism in early life. *W. Va. med. J.* **55,** 198–204.

POLLIN, W., STABENEAU, J. R., MOSHER, L. and TUPIN, J. (1966) Life history differences in identical twins discordant for schizophrenia. *Am. J. Orthopsychiat.* **36,** 492–509.

RACE, R. R. and SANGER, R. (1975) *Blood Groups in Man,* 6th edition. Blackwell, Oxford.

REYNELL, J. (1969) *Reynell Developmental Language Scales.* N.F.E.R., Slough.

RIMLAND, B. (1964) *Infantile Autism.* Appleton–Century–Crofts, New York.

14697610, 1977, 4, Downloaded from https://acamh.onlinelibrary.wiley.com/doi/10.1111/j.1469-7610.1977.tb00443.x by Universite Toulouse I Capitole, Wiley Online Library on [15/04/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

ROSE, A. L. and LOMBROSO, C. T. (1970) Neonatal seizure states: a study of clinical, pathological and electroencephalographic features in 137 full-term babies with a long-term follow-up. *Paediatrics* **45,** 404–425.

RUTTER, M. (1967) Psychotic disorders in early childhood. In *Recent Developments in Schizophrenia* (Edited by COPPEN, A. and WALK, A.). *Br. J. Psychiat., Spec. Publ.* **1,**

RUTTER, M. (1970) Autistic children: infancy to adulthood. *Seminars in Psychiatry* **2,** 435–450.

RUTTER, M. (1971) The description and classification of infantile autism. In *Infantile Autism* (Edited by CHURCHILL, D. W., ALPERN, G. D. and DE MEYER, M. K.), pp. 8–28. C. C. Thomas, Springfield, IL.

RUTTER, M. (1972) The effects of language delay on development. In *The Child with Delayed Speech* (Edited by RUTTER, M. and MARTIN, J. A. M.), pp. 176–188. SIMP/Heinemann Medical, London.

RUTTER, M. (1974) The development of infantile autism. *Psychol. Med.* **4,** 147–163.

RUTTER, M. (1977) Infantile autism and other child psychoses. In *Child Psychiatry: Modern Approaches* (Edited by RUTTER, M. and HERSOV, L.). Blackwell Scientific, Oxford.

RUTTER, M., BARTAK, L. and NEWMAN, S. (1971) Autism—a central disorder of cognition and language? In *Infantile Autism: Concepts, Characteristics and Treatment* (Edited by RUTTER, M.), pp. 148–171. Churchill–Livingstone, Edinburgh.

RUTTER, M., GREENFELD, D. and LOCKYER, L. (1967) A five to fifteen year follow-up of infantile psychosis—II. Social and behavioural outcome. *Br. J. Psychiat.* **113,** 1183–1199.

SEIDAL, U. P. and GRAF, K. A. (1966) Autism in two brothers. *Med. Offr.* **115,** 227–229.

SHERWIN, A. C. (1953) Reactions to music of autistic (schizophrenic) children. *Am. J. Psychiat.* **109,** 823–831.

SLATER, E. and COWIE, V. (1971) *The Genetics of Mental Disorders.* Oxford University Press, Oxford.

SMITH, C. (1974) Concordance in twins: methods and interpretation. *Am. J. hum. Genet.* **26,** 454–466.

STEVENSON, J. and RICHMAN, N. (1977) Behaviour, language and development in three-year-old children. *J. Autism Childhood Schizophrenia,* in press.

STUTSMAN, R. (1948) *Guide for Administering the Merrill–Palmer Scale of Mental Tests.* World Books. New York.

STUTTE, H. (1960) Kinder und Jugend psychiatrie. In *Psychiatrie der Gegenwort,* Vol. II (Edited by GRUHLE, H. W. and MAYER-GROSS, W.). Springer, Berlin.

TAFT, L. T. and COHEN, H. J. (1971) Hypsarrhythmia and infantile autism: a clinical report. *J. Autism Childhood Schizophrenia* **1,** 327–336.

TORREY, E. F., HERSH, S. P. and MCCABE, K. D. (1975) Early childhood psychosis and bleeding during pregnancy: a prospective study of gravid women and their offspring. *J. Autism Childhood Schizophrenia* **5,** 287–298.

TREFFERT, D. W. (1970) Epidemiology of infantile autism. *Archs gen. Psychiat.* **22,** 431–438.

VAILLANT, G. E. (1963) Twins discordant for early infantile autism. *Archs gen. Psychiat.* **9,** 163–167.

VAN KREVELEN, D. A. (1963) On the relationship between early infantile autism and autistic psychopathy. *Acta paedopsychiat.* **30,** 303–323.

VAN KREVELEN, D. A. and KUIPERS, C. (1962) The psychopathology of autistic psychopathy. *Acta paedopsychiat.* **29,** 22–31.

VERHEES, B. (1976) A pair of classically early infantile autistic siblings. *J. Autism Childhood Schizophrenia* **6,** 53–60.

WARD, T. F. and HODDINOTT, B. A. (1962) Early infantile autism in fraternal twins. *Can. Psychol. Ass. J.* **7,** 191–195.

WEBER, D. (1966) Zur Atiologie autistischer Syndrome des Kindesalters. *Praxis der kinder psychologie und kinder psychiatrie,* **15,** 12–18.

WECHSLER, D. (1949) *Wechsler Intelligence Scale for Children.* The Psychological Corporation, New York.

WHITTAM, H., SIMON, G. B. and MITTLER, P. J. (1966) The early development of psychotic children and their sibs. *Dev. Med. Child Neurol.* **8,** 552–560.

WILLERMAN, L. and CHURCHILL, J. A. (1967) Intelligence and birth weight in identical twins. *Child Dev.* **38,** 623–629.

WING, L., YEATES, S. R., BRIERLEY, L. M. and GOULD, J. (1976) The prevalence of early childhood autism: comparison of administrative and epidemiological studies. *Psychol. Med.* **6,** 89–100.

14697610, 1977, 4, Downloaded from https://acamh.onlinelibrary.wiley.com/doi/10.1111/j.1469-7610.1977.tb00443.x by Universite Toulouse 1 Capitole, Wiley Online Library on [15/04/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.

14697610, 1977, 4, Downloaded from https://acamh.onlinelibrary.wiley.com/doi/10.1111/j.1469-7610.1977.tb00443.x by Université Toulouse 1 Capitole, Wiley Online Library on [15/04/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License