

Monozygotic Twins Concordant for Infantile Autism : Follow-up

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This paper presents a well-documented case of monozygotic male twins concordant for infantile autism, with a twelve-year follow-up. Assessments include birth records, laboratory studies, physical measurements, psychometrics and quantifiable behavioural ratings by independent raters using multiple scales. Possible aetiological factors of infantile autism, as well as outcome are discussed.

Introduction

Although twin studies comprise a valuable portion of the research literature on the aetiology of schizophrenia in adults, no such studies have been conducted on psychotic children, with the exception of one by Kallmann and Roth (1956) on 52 pairs of twins with pre-adolescent (childhood) schizophrenia and one by Folstein and Rutter (1977), a retrospective but systematic and rigorous study of 21 pairs of same-sexed autistic twins. The literature relevant to autism in twins has been recently reviewed in Folstein and Rutter's paper and also by McQuaid (1975).

The twins to be described here constitute the twenty-ninth well-documented autistic pair and the seventh monozygotic pair concordant for autism.

Although there are a few well-conducted follow-up studies of autistic children (DeMyer *et al.*, 1973; Eisenberg, 1956; Kanner, 1971; Lockyer and Rutter, 1969; Lotter, 1974; Rutter, Greenfeld and Lockyer, 1967), our work represents the first study of such twins by long-term follow-up.

Case Report

The pair, Caucasian twin males, were referred for evaluation and treatment of slow development, including delayed speech and severely disturbed behaviour at the age of three years and ten months.

Developmental history

The children were the product of their mother's second, full-term pregnancy. There had been vomiting and a 3.63 kg weight loss in the first trimester, and it was reported that 'only one foetal heart was heard'. Twin A was born first, with a birth weight of 2.72 kg. Twin B was born 17 minutes later; he was a frank breech spontaneous delivery, weighed 2.61 kg, and required placement in isolette with full humidity because of slight cyanosis. The twins were discharged on the tenth day; weights were 2.92 kg and 2.81 kg respectively.* Motor development was uneven. The twins sat at four months, stood with support at four to five months and walked at about 14 to 16 months. By two years of age, both were over-active and destructive, tearing their playpen apart. At about three years of age, twin A became so hostile and aggressive toward twin B that separate bedrooms were required.

At approximately two years of age, twin B spoke his first word, 'Tide', in response to a child asking, 'What gets clothes cleaner?' He later acquired some other words, although he would not speak for weeks at a time. Twin A's language development remained arrested, and subsequently he became mute.

At approximately two to two and a half years of age, twin A became 'preoccupied' with his

* Data obtained from birth records.

hands and fingers, looking at them and playing with them. He would also keep staring through the window. He played with strings, tied belts, put his hands over his ears, and would sit in the corner in a 'prenatal position', oblivious to his surroundings. He developed insomnia and would cry at night. He had many fears, often transient. Twin B also became more withdrawn and exhibited a 'bad temper'.

Both children fed themselves from the age of one year with their fingers. Eating grass and smearing faeces were reported. They were not toilet trained.

Family history

The parents are a college-educated, upper middle-class couple, free of gross psychopathology; both are very concerned about the twins. A five and a half year old brother had been diagnosed elsewhere as 'brain damaged and hyperactive'.

Psychiatric evaluation

The twins were admitted to the psychiatric nursery at the age of 3 years 10 months. They were good-looking and well-developed youngsters. Twin B's body was covered with scratches from twin A's nails.

Both twins were withdrawn, twin A more than twin B. Eye contact was rare or fleeting. Both were stereotyped, negativistic or elusive. Their affect ranged from apathy to irritability. Motor activity ranged from over-activity to under-activity and anergy. Both would attack or bite themselves. Twin A showed no interest for inanimate objects, except for mouthing or biting them. His language consisted of some vocalizations; there was no evidence of language comprehension. In contrast, twin B had some adaptive skills; he had a few words, though his speech was echolalic, and he comprehended a few simple commands. Their intellectual functioning was retarded and uneven (see Table I).

Pertinent findings

The results of the work-up are shown in Table I.

Genetic work-up. On the basis of the criteria provided by the similarity method (including

haematological tests), qualitative and quantitative dermatoglyphic analysis, and anthropometric data, the twins were classified as monozygotic.*

Diagnosis of Schizophrenia, Childhood Type (DSM II, 1968) with autistic features, was made by Drs Barbara Fish, Theodore Shapiro, and the senior author. This diagnosis corresponds to early infantile autism as defined by Kanner (1943) and further delineated by Rutter (1967, 1976). Twin A had all nine, and twin B, seven, of the 'Nine Points' (Creak, 1964). The diagnosis of autism was subsequently confirmed by three other child psychiatrists and by Dr Leo Kanner.

Hospital course

The twins stayed in the nursery for 11 months. Response to the intensive therapeutic programme (milieu therapy and special education) was minimal in terms of improvement in socialization, language or patterned behaviour. Neither twin showed a response to psychoactive medication indicative of a meaningful acceleration in development. They remained essentially unchanged, thus requiring residential care.

Interim history

After their discharge the children were enrolled in a special day school. Twin A was placed into a residential treatment centre three months, and twin B two years, later. For the past eight years they have been together. At some point, twin B stopped talking, but he started again at the age of 14 years.

The twins' older brother is now in high school, a straight 'A' student, gifted in languages and writing. A fourth child, six years younger than the twins, had no reported problems. Both parents are well adjusted and working.

Follow-up

At the time of follow-up the twins were 15½ years of age. As shown in Table II, twin A was small and of light weight (1 kg lighter and only 7.6 cm taller than his nine-year-old

* Analyses were done by the associates of the late Dr Franz J. Kallmann, Department of Medical Genetics, New York State Psychiatric Institute.

TABLE I
Pertinent findings on initial evaluation*

| Parameters | Twin A | Twin B |
|--|--------------------|---|
| Weight/kg | 17.24 | 17.58 |
| Height/cm | 100 | 103 |
| Head circumference/cm | 51 | 51 |
| Chest | 58 | 56 |
| Abdomen | 58 | 57 |
| Intermittent concomitant strabismus .. | Right eye | Left eye |
| X-rays | | |
| Wrist for bone age | | <i>Identical:</i> Only 2 carpal bones, delay |
| Long bone series | | Normal |
| Blood lead** | 0.06 mg/100 g | 0.03 mg/100 g |
| Blood grouping | | <i>Identical:</i> |
| | A—Positive | M—Negative |
| | ABO—A ₁ | N—Positive |
| | Rh—Positive | Lewis—Negative |
| | Duffy—Negative | Kidd—Negative |
| | Kell—Negative | Lutheran—Negative |
| | S—Negative | U—Positive |
| | P—Negative | H—Negative |
| | | Cellano—Negative |
| Gesell Developmental Schedules | | |
| Motor | DQ = 46 | 21-30 months |
| Adaptive | <48 weeks | 30-36 " |
| Language | <40 " | 15 " |
| Personal-Social | 36 " | 15-30 " |

* Chronological age = 3-10/12 years.

** In whole blood, 0-0.05 mg/100 g.

brother). He had no facial or axillary hair and no hair on his extremities. Pubic hair was sparse, of semicircular shape, and about 1.25 cm in width. Testicles were descended. Both testicles and penis were undersized. He had facial asymmetry (right half of face lower than left). His wrists were covered with calluses as a result of biting. Twin A remained a withdrawn child, never making eye contact. Occasionally he would sit on an adult's lap, exploring or touching his or her face. He ignored his twin brother. He exhibited numerous mannerisms and rocked on his feet. Attention span was very short and some distractibility was noted. Negativism was mild, but elusiveness was severe. Language consisted of sparse vocalizations, imitations of sounds ('b' and 'm'), and comprehension of only a few words. He responded to his name inconsistently. Affect was flat. Motor activity ranged from under- to over-activity. He was ambidextrous. Muscle tone was good, with the exception of the thenar and

hypothenar which were underdeveloped, almost flat, with wrinkled skin over the palms.

Twin B was well-developed, muscular, 13 cm taller and 12.92 kg heavier than his twin (see Table II). Like twin A, he had facial asymmetry but with left half of face lower than right, thus exhibiting facial asymmetry reversal. He had some fine hair above his upper lip but none in the axillae. Hair was developed on the lower extremities. Pubic hair was normally developed but of female distribution. Testicles were descended and the penis was fairly well developed.

Twin B was also withdrawn and made no eye contact. However, he occasionally initiated physical contact. He had numerous mannerisms, though rocking was not observed. He frequently bit his lips. Twin B was moderately distractible, but his attention span was fairly good. He was very cooperative. Language consisted of words and some poorly phrased sentences, and he understood simple commands or questions.

TABLE II
Longitudinal data on the growth of the twins

| | Birth | | Chronological age in years | | | |
|----------------------------|--------|--------|----------------------------|--------|---------|--------|
| | Twin A | Twin B | 3-10/12 | | 15-6/12 | |
| | | | Twin A | Twin B | Twin A | Twin B |
| Weight/kg | 2.72 | 2.61 | 17.24 | 17.58 | 35.27 | 48.19 |
| Length/cm | 46 | 46 | | | | |
| Height/cm | | | 100 | 103 | 152 | 165 |
| Head circumference/cm .. . | | | 51 | 51 | 55 | 55 |

Speech was disconnected, autistic, and occasionally echolalic. He was unable to pronounce certain sounds (e.g. 'r'). In addition, his voice lacked inflection and was extremely mechanical. He spoke as if he had a strange, unidentifiable foreign accent. The most striking feature of twin B's speech was his tendency to sudden exclamations, apparently unrelated to the situation (e.g. 'fire department', 'money-bank' and 'wao-we'). Thinking was extremely concrete. Concepts were rudimentary or absent. Affect was flat. Facial expression was blank, although not as vacant as twin A's. He smiled frequently, although in a mechanical, stereotyped and often inappropriate manner. Occasionally he would burst into unexpected, inappropriate laughter. His motor activity ranged from under-activity to sudden outbursts of over-activity, with very rapid movements. He was right-handed and well coordinated.

The twins exhibited identical postures when sitting in an arm chair. When observed together among peers, their withdrawal was most striking.

Children's Behaviour Inventory (CBI). The CBI (Burdock and Hardesty, 1967), a standardized (normal population) observational instrument, was one measure used to assess the degree and quality of psychopathology at follow-up.

The twins were observed by independent raters, each of whom had attained interclass correlations of inter-rater agreement of at least .80. Although twin B was more developed than twin A (e.g. language skills, interpersonal relatedness), their behavioural profiles were strikingly similar.

Twin B had a total of 26 items scored for presence of psychopathology, while twin A had

27. Moreover, the twins had 13 of the same items. As can be seen in Fig 1, each boy had clusters of behaviours indicative of significant psychopathology in six sub-areas (standard score > 1.000) with four sub-areas in common: (a) Conceptual Dysfunction (disturbances of speech, memory or orientation), (b) Incongruous Behaviour (behaviours which are inconsistent with one another or with age norms, or are unusual ways of doing things), (c) Lethargy-Dejection (reflected in physical and emotional expression), and (d) Self-Depreciation (feelings of guilt, inferiority or worthlessness). In addition, twin A had scores indicative of Anger-Hostility (reflective in verbalizations or actions) and Incongruous Ideation (bizarre emotional and cognitive behaviours), while twin B received significant scores in Fear-Worry (indexes of anxiety) and Physical Complaints. It is interesting that although twin B had greater facility

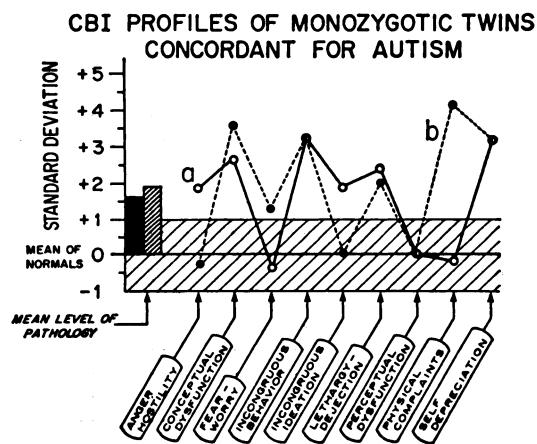


FIG 1.

with language than twin A, the quality of his communication skills was scored as disturbed (e.g. inarticulate, slurred and uneven speech). Psychiatrist's ratings (Children's Psychiatric Rating Scale) corroborate speech development problems in both boys (twin B estimated at 46-60 per cent developed; twin A estimated at less than 15 per cent). While the scores reflect some differences in functioning, overall assessment of CBI profiles and level scores (mean values) leads to an impression of severe disturbance, indicative of psychosis in children.

Children's Psychiatric Rating Scale (CPRS). The CPRS, developed by the Psychopharmacology Branch of the National Institute of Mental Health (*Psychopharmacological Bulletin*, 1973), was also used to evaluate the twins' behaviour. The 28 items which comprise the CPRS cover such areas as language development and pro-

duction, affect and motor functioning. Each boy was rated while being observed and interviewed by a psychiatrist. The quality of each behaviour was determined by its assignment to one of eight categories on a scale ranging from 'not assessed' to 'extremely severe'. None of the ratings were in the 'not assessed' category. Collapsing the remaining seven rubrics into not present, very mild-mild, moderate-moderately severe, and severe-extremely severe, highlights both disturbed functioning and basic similarities in the twins' repertoires. In particular, the items in common in the most pathological grouping (i.e. withdrawal, disorientation, unspontaneous relation to the examiner, blunted affect and other speech deviances) reflect significant dysfunctioning. Moreover, these common items are subsumed under the Nine Points (Creak, 1964) used to distinguish psychosis in children.

TABLE III
Comparison of twins at follow-up on Children's Psychiatric Rating Scale (CPRS)

| Item | Not present | Very mild-Mild | Moderate-Moderately severe | Severe-Extremely severe |
|--|-------------|----------------|----------------------------|-------------------------|
| 1. Tension | AB | — | — | — |
| 2. Unproductive speech | — | B | — | A |
| 3. Fidgetiness | — | — | AB | — |
| 4. Overactivity | — | B | — | A |
| 5. Underactivity | — | AB | — | — |
| 6. Distractibility | — | — | AB | — |
| 7. Abnormal object relationships | B | — | A | — |
| 8. Withdrawal | — | — | — | AB |
| 9. Over-compliant | AB | — | — | — |
| 10. Negative, uncooperative | B | A | — | — |
| 11. Angry affect | AB | — | — | — |
| 12. Silly affect | — | A | B | — |
| 13. Confusion | AB | — | — | — |
| 14. Disorientation | — | — | — | AB |
| 15. Clinging behaviour | — | B | A | — |
| 16. Unspontaneous relation to examiner | — | — | — | AB |
| 17. Suspicious affect | AB | — | — | — |
| 18. Depressed demeanour | AB | — | — | — |
| 19. Blunted affect | — | — | — | AB |
| 20. Lability of affect | — | AB | — | — |
| 21. Pressure of speech | A | B | — | — |
| 22. Level of speech development | — | — | B | A |
| 23. Stuttering | AB | — | — | — |
| 24. Low voice | A | B | — | — |
| 25. Loud voice | — | AB | — | — |
| 26. Mispronunciations | A | — | B | — |
| 27. Other speech deviance | — | — | — | AB |
| 28. Rhythmic motions (stereotype) | — | — | B | A |

In general, these data indicate that twin A is somewhat more deviant than twin B. However, the authors feel the most compelling finding is that, in spite of various differences in maturation and severity of illness, the boys exhibit similar behavioural indices of psychotic dysfunctioning.

Intelligence testing. Twin A displayed, on the Gesell Developmental Schedules, an upper range of gross motor functioning at the 48-month level, fine motor skills at the 36-month level, productive language at the 36-week level, and incalculably higher receptive speech. He could not be evaluated on the Stanford Binet because of failure to perform successfully all two-year level tasks.

Twin B was administered the Wechsler Intelligence Scale for Children (WISC). He scored in the middle of the Mentally Defective range of functioning, with a Verbal IQ of 46, Performance IQ of 52, and Full Scale IQ of <42. His mean mental age was 6 years 9 months.

Comments

As indicated in other major follow-up studies of autistic children (Eisenberg, 1956; Lockyer and Rutter, 1969), the level of intellectual functioning tends to remain stable over the years. This stability is apparent in this pair of twins. In spite of differences in their IQs, the severity of psychosis assessed on follow-up as reflected in behavioural ratings was almost identical. Thus it is possible that in addition to IQ the degree of psychosis, too, is influential in determining the course of the syndrome. Other investigators (Folstein and Rutter, 1977) have also found similar behavioural patterns in monozygotic twins concordant for autism, in spite of discrepancies in the intellectual quotients.

As in other studies, the differences between this monozygotic twin pair are more interesting than the similarities. For example, while at birth twin A, the first born, was the heavier, by the age of 3 years 10 months, he was lighter, somewhat shorter, and developmentally more retarded than twin B. The physical discrepancy became magnified over the years, although the twins remained in the same environment (except for two years of interruption). Thus, it appears

that the concept of biological age (Cheek, Migeon and Mellits, 1968) is applicable in this case, as physical maturation (including somato-sexual), severity of psychosis, and degree of retardation are correlated.

As far as the causation of autism is concerned, little is known. However, it is believed that this clinical picture is probably aetiologically heterogeneous (for review see Ornitz, 1973; Ritvo, 1976; Rutter, 1967).

Of the 11 pairs of monozygotic twins in Folstein and Rutter's study, 4 were concordant for autism, while it is estimated that only about 2 per cent of the siblings of autistic children develop the same condition (Hanson and Gottesman, 1976; Rutter, 1967).

Perinatal complications are more common in multiple than in single births (Dunn, 1965), and are more common in autistic children *per se* (Campbell, unpublished work; Folstein and Rutter, 1977; for review see Campbell, 1977; Torrey, Hersh and McCabe, 1975). In the case of the present pair, twin B, the less impaired of the two, was the one who probably suffered such insult to the CNS. He was born 17 minutes after twin A, had frank breech delivery, was slightly cyanotic and was slightly lighter than his brother. The older brother of the twins, too, had certain difficulties as a child, including language, motor activity and visuo-motor functions. Folstein and Rutter on the basis of their study of 21 twin pairs, their siblings and parents hypothesize that a form of cognitive-language deficit operative in, but not restricted to, autism is genetically determined. They suggest that autism develops as a result of a genetic predisposition and biological hazards, including perinatal brain damage. This interesting concept has supportive evidence (Campbell, unpublished work; Vaillant, 1963) and merits further investigation.

Clearly, in addition to biochemical and other investigations, thorough genetic and longitudinal studies are needed in order to identify aetiology, more precisely define diagnostic criteria and introduce more effective treatments in infantile autism. Genetic twin studies, especially of a longitudinal design, would appear to be a methodological step in the right direction.

Acknowledgements

This study was supported in part by Public Health Service Grant MH-04665 from the National Institute of Mental Health. At the time of follow-up, Dr Dominijanni was a post-doctoral Fellow. The authors wish to express their thanks to Mrs Nancy T. Polevoy for organizing the follow-up.

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(Received 7 December 1976; revised 4 March 1977)

BJPpsych

The British Journal of Psychiatry

Monozygotic twins concordant for infantile autism: follow-up.

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BJP 1977, 131:616-622.

Access the most recent version at DOI: [10.1192/bjp.131.6.616](https://doi.org/10.1192/bjp.131.6.616)

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