twins—still our best method*

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The field of schizophrenia continues to be the battlefield for conflicting theories in psychiatry. Until recently, the psychiatric establishment held the view that schizophrenia was a genetic disease. In the mid-1960's, this view changed, partly because of new twin studies that deemphasized the genetic component. The humanistic-existential movement, family hypotheses, and emphasis on social processes gave additional support to an environmental and developmental view of schizophrenia. During recent years, the pendulum has swung back to the hereditary point of view.

The New Adoption Studies

Gottesman and Shields (1976) present a valuable summary of the American-Danish adoption studies. Several reports of this impressive project have appeared, but we still lack the final report that should present, in detail, design, sample, and results. Personally, I am very much impressed with the elegant experimental design of these studies. I am less impressed, however, by the way these studies have been "propagandized." One has the feeling that results from twin research have been completely ignored. The adoption method was not invented by the group; it has been used before. Nor has it been possible to separate completely "pathological genes" from "pathological milieu" through these studies. There are problems, of course, and sources of errors in twin studies, but they are still our best method in heredity-environment research. My prediction is that the problems encountered in twin studies are slight compared with the problems adoption studies will face. The Gottesman and Shields review clearly displays all the uncertainties that surround these studies. Let me briefly underline some of the relevant factors with regard to sampling and statistical significance.

**Sampling**

First, only definite parents were permitted to give their children up for legal adoption. Second, adoptive parents represent, as in most Western countries, a restrictive range of environment for the adopted child (cf. Kellmer-Pringle 1966). Third, one observes, as in most previous adoption studies, a correlation between socioeconomic status of the biological and the adoptive parents. Skodak and Skeels (1949) found that the children ending up in the better foster homes had true (biological) mothers with higher IQ's and more education. It is well known that selective placement takes place in the assignment of children to foster homes, particularly in terms of such variables as religion, family structure, values, and child-rearing practices. Often the staff members of private or public agencies seem to want to achieve some sort of fit between the child's background and his foster home. Finally, the spouses of schizophrenics whose offspring were adopted tend to be "sicker" than such spouses in general. Hence, they are not representative of the spouses of schizophrenics. It would appear that all of these weaknesses with regard to sampling lead to an overestimation of genetic factors.

**Statistical Significance**

A recurring problem in the American-Danish adoption studies is the small sample size. In table 2 of the
Gottesman and Shields review, percentages are given without actual number. In the "Kety strategy," for instance, 12.1 percent corresponds to only eight cases, 6.2 percent to four, 1.6 percent to one, and 4.4 percent to three cases. The differences reported between experimental and control groups are small and mostly not statistically significant. If typical schizophrenia is used as a discriminating factor, the differences are small indeed. The more pronounced differences, although not statistically significant, are arrived at by enlarging the concept of schizophrenia to a "schizophrenia spectrum" that includes not only typical schizophrenia, but also borderline cases, eccentrics, and patients with acute schizophrenic-like reactions. One might ask if this broadening of a diagnostic category has any heuristic value at all. In any event, their findings need replication since the definition of schizophrenia spectrum disorders seems to be somewhat unclear.

I agree with Gottesman and Shields that the extremely high rates of schizophrenia in the biological half siblings (Kety et al. 1975) is, from a genetic point of view, meaningless. It would appear to me that focusing attention on their life histories might be worthwhile—that is, focusing on their environment. Both Kety et al. and Gottesman and Shields are eager to discuss somatic environmental factors such as intrauterine factors, but why be afraid of the social milieu?

**Twin Studies**

Based on a summary of recent studies, I usually state that the concordance figures are 25-40 percent in monozygotic (MZ) and 5-15 percent in dizygotic (DZ) twins. To quarrel about "true" concordance is a waste of time, but to maintain, as Gottesman and Shields do, that concordance is 50 percent, and furthermore that the total difference in concordance between MZ and DZ twins is solely due to genetic factors, is unreasonable because of the following points:

- If one uses the direct pairwise concordance, which is simple and reasonable when comparing MZ and DZ twins, the four recent twin studies based on systematic sampling yield the concordance rates shown in table 1. As can be seen in the table, the concordance rate in MZ twins is on the average around 30-40 percent or less; in DZ twins, it is 10-12 percent. These are maximum figures, however, because of shortcomings in sampling. Let me illustrate my point by focusing attention on Gottesman and Shields' (1966) own study. They collected 24 MZ pairs of whom 10 were concordant and 14 discordant. In 4 out of 10 concordant pairs both partners were patients at Maudsley Hospital. In the remaining 6 pairs, the co-twin had been diagnosed as schizophrenic by followups of probands. It is evident that concordant pairs have a greater chance of appearing in a hospital sample than discordant ones. This can be shown mathematically in a simple way, particularly if the hospital sample is very small compared with the total twin population.

**Example:** If one assumes that the probability of being hospitalized and reported is 80 percent and that members of a concordant pair are admitted and reported independently, the probability of being in this sample is .8 for a discordant pair and .96 for a concordant pair. (The probability that either of two outcomes will occur is the sum of their probabilities, minus the probability that both will occur together. Thus for a concordant pair, $p = .8 + .8 - (.8 \times .8) = .96$.) If the probability of being hospitalized and reported is lower—for instance, 50 percent—the probability is .5 for a discordant pair and .75 for a concordant one. If the probability is as low as 10 percent, $p = .1$ and .2 (.19), respectively. This means that if the sample is so small that all the concordant pairs are represented solely by one affected partner, then the direct pairwise concordance rate will give the double concordance rate for the population, simply...
because concordant pairs have a double chance of being represented in the sample.

If Gottesman and Shields want to calculate the real pairwise concordance rate in the population, the 4 of their 10 concordant pairs can be counted fully, whereas 6 of the 10 pairs must be counted half. In other words, because of shortcomings in sampling, their 42 percent pairwise concordance should be corrected to 33 percent, a percentage that deviates considerably from the classical studies and is in accordance with more recent work.

- The total difference in concordance rate between MZ and DZ twins cannot be ascribed to genetic factors only. A series of studies of both normal and abnormal twins show that the environment of the MZ twin pair is more similar than the environment of the DZ twin pair.

How this might affect concordance is shown in a study of criminal twins by Dalgard and Kringlen (1976). In an unselected sample of 138 pairs of same-sexed male twins, age 40-50 years, who were obtained through the Norwegian national criminal register, concordance with respect to registered crime was slightly higher in MZ than in DZ twins. Employing a broad concept of crime, concordance was 22.4 percent in MZ and 18.0 percent in DZ twins. With a stricter concept of crime, concordance was 25.8 percent in MZ and 14.9 percent in DZ twins. Since MZ pairs experience a more similar upbringing than DZ pairs, the authors compared groups of MZ and DZ twins who by and large had been exposed to the same type of environmental influence in childhood and adolescence, such as being dressed alike and treated as a unit. In such a comparison, the difference in concordance almost completely disappears.

- There is, in fact, a difference in concordance rates between DZ twins and ordinary siblings. Whereas the pairwise method seems reasonable in comparing MZ and DZ twins, one should employ a casewise rate (proband method) for comparison of rates among siblings. In my own study, the rates for strict schizophrenia are 8.9 percent for DZ co-twins and 3 percent for siblings (of MZ twins). The rates given in my monograph (Kringlen 1967, table 57) are regrettably wrong, as pointed out by Anderson (1970).

An even more marked difference is to be found in Fischer's (1973) study. The concordance rate was as high as 26 percent (12/45) in same-sexed DZ twins compared with 10 percent (13/129) in same-sexed sibling pairs. I should like to add that Slater (1953) also found a higher concordance in DZ co-twins than in full siblings (14.4 as against 5.4 percent). Kallmann (1938) is in fact the only investigator who did not find any difference. (Tienari [1963 and 1975] and Gottesman and Shields [1966 and 1972] did not investigate siblings.) These findings are, in other words, rather consistent, and it is natural to attach significance to the observed differences. (One has to make one reservation—namely, that it is theoretically possible that the twins in the various samples have been more carefully investigated than the siblings, although Fischer denies this possibility with regard to her own sample.) The higher morbidity figures in DZ co-twins compared with the morbidity rates in siblings must be ascribed in part to the twinship itself. From a genetic point of view, one should expect to find the same concordance rate in DZ co-twins as in siblings.

In conclusion, because of shortcomings in sampling, which are even present in the modern studies—namely, differential environmental influences in MZ compared with DZ twins and higher concordance in DZ twins than in siblings—the concordance rates in several of the newer studies must be considered as maximum figures. Hence, to repeat over and over again, as Gottesman and Shields do in their review, that the twin studies from the 1960's are just replications of the older ones is nonsense. There is a remarkable difference, for example, between Kallmann's (1938) influential work and the newer series of twin studies where rates on siblings also have to be taken into account. If a concordance rate of 30 percent in MZ twins had the same meaning as a rate of 80 percent these studies would not have been carried out.

Gottesman and Shields praise themselves for having a broad outlook on schizophrenia. They even "acknowledge and . . . value the part played by external environmental and internal psychodynamic factors in the development of schizophrenia" (p. 360). Their belief, however, seems to be of a weak nature, because every time an alternative environmental explanation of data crops up, giving room for a tiny little environmental factor, the authors fall upon this poor factor and kill it. I had thought some of these meager factors might be present in the section on discordant twins, but the only factor invited to the geneticist's party is, comically enough, the submissive factor—he is the only psychodynamic guest in a party consisting of biochemical and physiological "endophenotypes."

It is true that our yield from the studies of discordance is limited. There are trends, however, that ought to have been reported in such a review, such as the suggestive findings of Wahl's (1976) review of MZ twins.
twins discordant for schizophrenia. The author concludes that life-history comparisons of schizophrenics with their nonschizophrenic co-twins have revealed consistent early differences in personality and parental treatment. Tienari (1963) also reported interesting data. He found that in 13 of 16 male cases the twin later to become schizophrenic seemed to have had a disturbed relationship with his father.

To take my own study (Kringlen 1967), I observed that MZ discordant schizophrenic twins seem to have been exposed to a more variable milieu than concordant pairs. Concordant pairs tended to have had less social contact with other children and thus less varied social experiences, to have been closer in childhood, to have been more overprotected, and to have been more often brought up alike by their parents. Discordant pairs, on the other hand, had been separated more often in childhood and for longer periods of time, and more frequently had received differential treatment and affection from their fathers, one member of the pair being favored. The data also indicated that concordant pairs seem to have faced more stressful as well as more similar environments. They tended to come from lower social classes and worse economic situations than their discordant counterparts, and they tended to be more socially isolated. I should of course add that the trends described are not statistically significant. The results, however, are consistent and clinically meaningful.

Misunderstandings?

Gottesman and Shields now and then speak about the “solution of the schizophrenia problem.” I think this is a misunderstanding of what we are dealing with. Just as there are no solutions to normal personality development, there will be no solution to the “schizophrenia riddle.” Schizophrenia is a way of life—an extreme one. We may therefore reach a deeper understanding of the schizophrenic and his world, we might be able to identify more and more causal connections, but I do not think we should expect a “breakthrough” within biological research, or social research for that matter.

The authors tell us that the adoption studies have ruled out alleged environmental factors. How? On the contrary, one could conclude that in addition to supporting genetic factors, they support environmental etiological factors. Rosenthal (1971) discusses why the morbidity rate of schizophrenics in the adoptee pool

was so low, namely .65 percent. (The morbidity risk for schizophrenia in Scandinavia is observed to be around .9 percent, with a range of .65-2.85 percent.) Either some children at risk were not given up for adoption, or as Rosenthal speculates, rearing by adoptive parents, also screened, might have protected vulnerable children.

Gottesman and Shields seem wrongly to identify a “schizophrenogenic” rearing with rearing by schizophrenic parents. From clinical work we know that the schizophrenogenic rearing in fact might be more pronounced in borderline families than in families with a clear-cut schizophrenic as a parent member. One should also remember that the majority of schizophrenics are born to clinically nonschizophrenic parents.

Conclusion

The Gottesman and Shields review covers such a broad area of schizophrenia research that it is impossible to deal with the subject in any detail within the scope of a short commentary. I have confined myself, therefore, to only a few of the central questions—in particular twin research where I am most at home. I have tried to state my disagreement with the authors as clearly as possible. Perhaps some readers who are not familiar with the field would have appreciated a more meticulous justification for some of my statements.

The main asset of the review to my mind is the authors’ summary of the newer adoption studies. The weakness of the review is its one-sidedness in that it leaves out too many alternative explanations. I have a feeling that the authors seem to avoid consistently any environmental explanation of data when such alternative interpretations are natural.

It is often stated today that there are no geneticists of the old school remaining, just as there are no extreme environmentalists any more. All are, or ought to be, research workers on interaction. After reading the Gottesman and Shields critique, I feel that we still have a few who are too much caught up in old ideas. That is a pity.

References


Dalgard, O. S., and Kringlen, E. A Norwegian twin


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Dr. David Rosenthal, Chief of the NIMH Laboratory of Psychology and Psychopathology and *Schizophrenia Bulletin* editorial advisory board member, has received a coveted Professional Achievement Award from the University of Chicago Alumni Association. Presented to Dr. Rosenthal at a special Alumni Reunion Luncheon at the University on June 5, the award is bestowed upon outstanding graduates whose achievements deserve special recognition.

Well known for his landmark studies of the adopted-away offspring of schizophrenics in Denmark, Dr. Rosenthal is regarded—to quote NIMH Director Bertram S. Brown—"as one of the top scientists in the area of the nature and etiology of schizophrenia."