

**TWIN STUDIES IN PSYCHIATRY  
AND NEUROPATHOLOGY**

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**The Unique Contribution of Twin Studies to  
the Elucidation of Nongenetic Factors  
in Personality Development and Psychopathogenesis****William Pollin**

Our Section in Bethesda is primarily engaged in studies of schizophrenia and personality formation. I will summarize a number of our ongoing studies, and then briefly focus on a methodological issue: the possibility of twin studies moving beyond their heretofore almost constant, very useful tie to genetic studies.

We have previously reported an elaborate multidisciplinary study of a series of MZ twins discordant for schizophrenia, a smaller number of appropriately matched control twin pairs, and their families, aimed at studying nongenetic factors in the pathogenesis of schizophrenia (Pollin et al, 1965, 1966). We have described three interacting groups of variables which consistently differentiated the schizophrenic and nonschizophrenic twins in the discordant pairs (Pollin and Stabenau, 1965). These included an initial set of nongenetic constitutional differences, including birth size, vigor, and physiological competence; consequent different parental perceptions of, and relationships to, each of the twins in a given pair; and subsequent biological and life history differences, based on evolving personality differences, such as in fearfulness, competence, independence, initiative and the like, differentiating the schizophrenic index and the nonschizophrenic cotwins.

At this point I wish to present one additional biochemical finding from this series. Dr. Kopin's laboratory measured a series of catecholamines: norepinephrine and epinephrine — their major precursor, dopamine — and their major metabolites. We also studied adrenal steroids. Catecholamine levels are related to the schizophrenic genotype; 17-hydroxy steroids, to the phenotype. This is most marked for epinephrine; a similar pattern is present for most other amines. Epinephrine values for both twins in concordant pairs, and both the schizophrenic and the nonschizo-

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phrenic cotwins in the discordant pairs, are all elevated; they differ from the values in the normal pairs at better than the 0.005 level. Conversely, 17-hydroxy steroid values are elevated in the schizophrenic index twin in the discordant pairs; however, the nonschizophrenic controls show essentially the same mean values as the normal twins ( $P < 0.02$ ). We are currently engaged in a more intensive analysis of the quantitative data from this study, analyzing the first of several 90 variable correlation matrices, which show an interesting relationship between observations from different disciplines (Pollin, 1970).

We plan a replication of the discordant pair study to eliminate sampling problems, and to introduce additional subseries of MZ pairs discordant for other psychopathologies, so as to determine which, if any, of our differentiating findings are specific for schizophrenia, rather than generally true of psychopathology. The initial source of our replication series will be a NRC panel of 15 909 pairs of male Veteran twins.

In our preliminary chart analysis of that series we found 338 pairs with one or both twins schizophrenic, 85% of them discordant. Despite the low overall concordance rate, in the 226 pairs of established zygosity, the age corrected pairwise concordance rate for schizophrenia was 15.5% for MZ and 4.4% for DZ twins, yielding an MZ/DZ concordance ratio of 3.4 (Hoffer et al, 1969). Similar analysis of the 1559 pairs showing psychoneurosis in the NRC sample yielded an MZ/DZ concordance ratio of only 1.3.

A reanalysis of 18 major twin studies which make possible the computation of similar MZ/DZ concordance ratios for schizophrenia and psychoneurosis shows a similar difference in MZ/DZ ratios in all but one instance, despite considerable variability of sampling and diagnostic criteria in the different studies (Fig. 1). Correlational analysis of the NRC sample, in which 14 diagnostic categories, 8 non-psychiatric, were analyzed, shows that part of this difference in MZ/DZ concordance ratios is inversely related to incidence. However, correcting for incidence discloses that the bulk of the difference is not related to incidence.

This significant and consistent difference between the MZ/DZ concordance ratio for schizophrenia, and that for neurosis, in all but one of 18 major twin studies, suggests the presence of a genetic factor in the pathogenesis of schizophrenia, and its relative absence in psychoneurosis. However, since approximately 85% of affected MZ pairs in the NRC sample are discordant for schizophrenia, the role of the suggested genetic factor appears to be a limited one (Pollin et al, 1969).

Now, the methodological point I referred to. Historically, twin studies have been associated predominantly with the study of genetic variables or of genetic-environmental interactions. The reasons for this powerful linkage are many and the rationale clear and justifiable. Nonetheless, it appears that the strength of this relationship has impeded an important alternative twin study application: the clarification of nongenetic etiologic factors. In such studies, certain twin populations

## NEUROSIS STUDIES:

Slater, 1953  
 Shields, 1954  
 Slater, 1961  
 Ihda, 1961  
 Braconi, 1961  
 Inouye, 1965  
 Parker, 1966  
 Pollin et al. 1969

## SCHIZOPHRENIC STUDIES:

Rosanoff, 1934  
 Essen-Möller, 1941  
 Kallman, 1946  
 Slater, 1953  
 Inouye, 1961  
 Tienari, 1963  
 Harvald and Hauge, 1965  
 Gottesman and Shields, 1966  
 Kringlen, 1967  
 Pollin et al, 1969

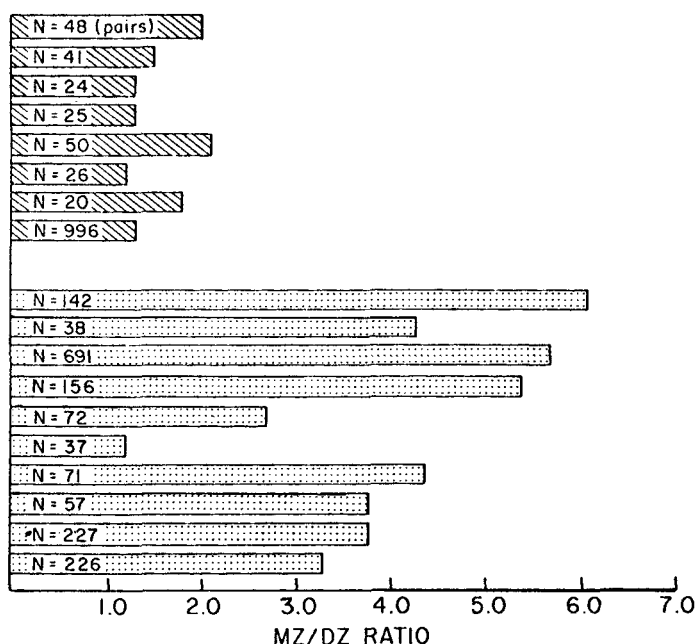


Fig. 1. MZ/DZ concordance ratios in twin studies of neurosis and schizophrenia (From Pollin et al, 1969).

can make a unique methodological contribution. This contribution results from the fact that MZ twins discordant for a given illness or discrepant for a given variable of a continuous nature provide a uniquely well matched control population. Such a level of matching, rarely attained in the biological sciences, constitutes in effect a qualitative rather than a quantitative advance. Discordant MZ twins are not only perfectly matched for genetic variables, but also for many other frequently relevant variables: ethnic, socioeconomic, chronological and similar factors. Because MZ pairs are similar in so many respects, the possible determinants of their discordance are sharply reduced in number, and correspondingly, the likelihood of identifying such determinants is increased. Our study of pairs discordant for schizophrenia is one example of such a study; let me describe an additional alternate model. Benjamin (1960) and Gifford et al (1966) have previously described similar investigations.

We are now in the pilot phase of a study of personality development, employing a small series of newborn MZ twins and their families. Mothers are referred when their obstetricians diagnose multiple pregnancy. Home family visits are made before birth and parental personality and family relationship defined. Birth is observed; if the twins are MZ, the family is included in the series, and followed by subsequent periodic home visits, diagnostic

and psychological tests, sound films and a still evolving research protocol. Our aim is to be able to define the earliest consistent differences in infant and child personality, and by relating these to differences in birth, constitution, intrafamilial relationships, and life experience, to cast light on some basic nongenetic determinants of personality formation.

Thus far, we are already impressed by the observation that within the narrowed range of similarity shown by MZ pairs, in most pairs one twin can be seen as more obsessive-compulsive, the other more hysteric; one more person oriented, the other more object oriented; one patiently exploring each new facet of the environment, the other hurriedly racing to always find some new stimulus; one more fearful, the other more confident and dominant. We expect to be able to find consistencies in the sources of such differences that would be extremely difficult to identify in any but an MZ twin population, and we would urge other twin investigators to explore the possibilities of similar nongenetic studies in twin populations.

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