

## Don Jackson's "A Critique of the Literature on the Genetics of Schizophrenia": A Reappraisal After 40 Years

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**ABSTRACT.** In 1960, Don Jackson published "A Critique of the Literature on the Genetics of Schizophrenia." Jackson's critique nearly relegated the classical twin method to obscurity as being hopelessly confounded by environmental factors. Jackson noted several trends in the schizophrenia twin data that were difficult to explain on genetic grounds. In fact, none of Jackson's 12 major points, examined in this article, have been satisfactorily answered by proponents of the twin method. The evidence in support of Jackson's most controversial claim—that the psychology of twinship itself might lead to a greater rate of schizophrenia among twins when compared with the single-born population—is inconclusive. However, although several leading twin researchers have dismissed Jackson's entire thesis on the basis of the inconclusiveness of this one claim, this idea was not central to Jackson's basic argument. The research undertaken for this article appears to confirm the validity of the most important points of Jackson's analysis and that therefore the classical twin method is of doubtful value as an indicator of genetic influences on schizophrenia and other diagnoses or psychological trait differences. Jackson's article demonstrated the implausibility of what came to be known as the MZ/DZ "equal environment assumption" of the twin method, implying that the twin method records nothing more than environmental differences between monozygotic and dizygotic twins.

**Key words:** Don Jackson, equal environment assumption, genetics, schizophrenia, twin method, twin studies

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**WE ARE CURRENTLY WITNESSING** an explosion in twin research. The published results of twin studies are found in the most prestigious journals in psychiatry, psychology, and the related fields and are cited as important evidence supporting a significant role of genetic factors for a wide range of psychiatric disorders and psychological traits. Twin research has attained a legitimacy never before enjoyed, but there was a time not long ago when it was considered a vir-

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tual pseudoscience. This was due in part to the work of one man, who in 1960 wrote the most important critique of twin research ever published.

The author of the article was Don Jackson, then Director of the Mental Research Institute in Palo Alto, California. Its title was "A Critique of the Literature on the Genetics of Schizophrenia" (Jackson, 1960). Jackson was a well-known pioneer of family systems theory and had been a co-author of a widely discussed article outlining the "double-bind" theory of schizophrenia (Bateson, Jackson, Haley, & Weakland, 1956). In a sense, Jackson's critique is a forgotten document today; although widely discussed in the 1960s, it has been largely ignored or overlooked since that time.

At the time of Jackson's article there were five published schizophrenia twin studies; Kallmann's (1946) report was the most prominent. These studies were based on the "classical twin method," which compares the concordance rates or correlations of reared-together identical twins (monozygotic, or MZ; 100% genetic similarity) with the same measures of reared-together same-sex fraternal twins (dizygotic, or DZ; 50% genetic similarity on average). According to twin researchers, a significantly greater MZ concordance rate, when compared with same-sex DZs, is attributable to the greater genetic similarity of MZ twins. Jackson argued that the methodologies of the five twin studies were flawed and that their findings contained trends that were difficult to explain from the genetic standpoint. He suggested that the unique psychological bond and greater environmental similarity experienced by monozygotic twins could explain their higher concordance rate when compared with dizygotic twins.

Jackson's article had an important impact on the debate over the causes of schizophrenia and raised serious doubt that the twin method measured anything other than the close association and "ego fusion" of twins. In the period following the publication of his article, twin researchers carefully considered his observations and attempted to improve the methodology of their studies. But most failed to understand that the implication of Jackson's critique was not that the twin method was in need of methodological improvement, but rather that its logic was erroneous at the core level.

By the mid-1970s, however, Jackson's arguments were largely ignored as the twin method regained its foothold as an accepted research method. Jackson's main interest was family systems theory, and he did not become an important figure in the nature/nurture debate after 1960. We do not know if Jackson would have elaborated on his views in the 1970s and after, as he died prematurely in 1968.

In their 1972 book on the genetics of schizophrenia, twin researchers Gottesman and Shields were prepared to relegate Jackson's critique to the status of a historical footnote:

[In 1960] came the book edited by Jackson. . . . *The Etiology of Schizophrenia*, containing a critique by him of the "literature of the genetics of schizophrenia." Even today, a decade later, the chapter is considered in many quarters to be the definitive

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rebuttal to genetic thinking and an excuse to ignore any developments generated by genetic hypotheses; the critique dealt especially harshly with Kallmann's (1938, 1946) findings and conclusions. . . . Although a few of Jackson's points were well taken, most have since been shown to have no force. . . . (1972, p. 4)

Ten years later, Jackson was viewed by Gottesman and Shields as little more than a "vocal critic of genetic interpretations" (1982, p. 73).

What follows is a review of Jackson's basic arguments and an examination of the ways that advocates of the genetic position attempted to answer them. There are 12 major points raised in Jackson's article and while all did not originate with him, together they make a strong case that genetic studies of schizophrenia (and twin studies in particular) contained serious and invalidating flaws.

The first schizophrenia adoption study (Heston, 1966) appeared 6 years after the publication of Jackson's article and was therefore not part of his analysis. Jackson's major points were as follows:

1. In discussing family (consanguinity) studies, it was noted that conditions can run in families for environmental reasons.

2. There were no genetic studies of schizophrenia in which diagnoses had been made blindly. The results of these studies were therefore susceptible to the researchers' bias.

3. There were other sources of bias in the diagnostic process such as the unreliability of schizophrenia diagnoses and the finding that people had a better chance of being diagnosed with schizophrenia the longer they stayed in the hospital. An important sampling bias was introduced by the methods used to obtain twin subjects, which could lead to inflated concordance rates.

4. Contrary to genetic expectations, DZ twins were more concordant than siblings even though they had the same genetic relationship to each other.

5. Contrary to genetic expectations, female MZ twins (MZf) were more concordant than male MZ pairs (MZm).

6. Contrary to genetic expectations, female DZ pairs (DZf) were more concordant than male DZ pairs (DZm).

7. Contrary to genetic expectations, same-sex DZ twins (DZss) were more concordant than opposite-sex DZs (DZos).

8. Individual case histories of reared-apart MZ twins concordant for schizophrenia do not provide important evidence for genetic factors because they were few in number (two), and the pairs grew up in similar environments and had an interactive relationship with each other.

9. Monozygotic twins grow up in a more similar environment and are treated more similarly than dizygotic pairs. Therefore, greater MZ similarity or concordance could be explained by the more similar environment they experience.

10. Contrary to the genetic hypothesis, the psychodynamic thesis predicts that concordance rates should correlate with the degree of likeness among siblings, regardless of their genetic relationship.

11. The unique psychological bond or "ego fusion" of MZ twins contributes to a higher MZ concordance rate for schizophrenia on the basis of association and identification. Furthermore, the identical twinship itself might create conditions leading to the identity problems often experienced by people diagnosed with schizophrenia.

12. There is a striking similarity between reports of folie à deux (shared psychotic disorder) and the case histories of MZ twins concordant for schizophrenia.

We will look at the ways that leading proponents of the twin method responded to Jackson, by concentrating on his 12 major points and going into detail when necessary. The most important response to Jackson's critique was provided by David Rosenthal in a series of publications (1960, 1961, 1962a, 1962b). These articles were frequently cited by twin researchers attempting to counter Jackson's theories and are discussed when relevant.

1. *In discussing family (consanguinity) studies, it was noted that conditions can run in families for environmental reasons.* Today there is little disagreement with this observation, although in the past consanguinity studies were held up as important evidence for the operation of genetic factors. Kallmann, for example, viewed the results of his consanguinity study as providing "conclusive proof" of the genetic basis of schizophrenia (1938, p. xiv), whereas most modern psychiatric geneticists acknowledge that family studies offer only an "initial hint" that a condition might have a genetic basis (Faraone & Tsuang, 1995, p. 88).

2. *There were no genetic studies of schizophrenia in which diagnoses had been made blindly. The results of these studies were therefore susceptible to the researchers' bias.* This problem was acknowledged by Rosenthal (1962b) and others as a potential bias. Rosenthal recommended that "In future investigations" there should be "no person making the psychiatric diagnosis of both members of any given pair. There should be no communication about cases among investigators . . ." (1962b, p. 126). Gottesman and Shields' schizophrenia twin study (1972) employed a panel of judges who diagnosed blindly from records assembled by the researchers. Gottesman and Shields concluded that the older studies had not been seriously biased by non-blinded diagnoses. Although more could be said about this issue, it is sufficient to note that, in general, twin researchers now acknowledge that blind diagnoses are preferable to non-blind diagnoses.

3. *There were other sources of bias in the diagnostic process such as the unreliability of schizophrenia diagnoses and the finding that people had a better chance of being diagnosed with schizophrenia the longer they stayed in the hospital. An important sampling bias was introduced by the methods used to obtain twin subjects, which could lead to inflated concordance rates.* The truth of these observations is generally acknowledged by modern twin researchers, although the older studies have been defended (see, for example, Shields, Gottesman, & Slater, 1967).

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There are three main ways in which twin subjects have been obtained: the resident hospital method, the consecutive admissions method, and the register method.<sup>1</sup> In the first method, the records of psychiatric hospital patients diagnosed with schizophrenia are examined. The researcher then attempts to discover if any of these patients are members of a twin pair. After a subject is found in this way, the researcher attempts to locate the co-twin of the affected person. The zygosity (genetic relationship) of the pair is then determined, after which a diagnosis of the co-twin is made. Typically, the same researcher makes the diagnosis for both members of the pair. Sometimes a twin pair will be located because the researcher has been told of the existence of a schizophrenic twin by a person connected with a particular hospital.

The resident hospital method was employed in several of the earlier studies (Kallmann's 1946 study being the most prominent). Since the 1960s there has been widespread agreement among twin researchers that this method creates a sample biased in favor of concordance. Rosenthal (1962b) discussed some of the problems in obtaining twin samples from resident hospital populations. First, many people diagnosed with relatively mild cases of schizophrenia are never hospitalized, which skews the sample toward the most severely affected, who are known to be more concordant than those with milder conditions. Second, after obtaining subjects from the hospital population, continued Rosenthal, the researcher must then undertake the difficult task of locating the subject's co-twin. In some cases this twin will be dead or impossible to locate. Third, because most twin samples are small, "the tendency then is to retain as many pairs as possible by getting as much information as one can about all pairs of twins and making one's best judgment about zygosity and concordance for each pair" (Rosenthal, 1962b, p. 121). Thus, pairs lacking sufficient information for accurate zygosity determination or diagnosis have been retained in several studies in order to maintain requisite sample sizes.

As noted by the authors of a textbook on schizophrenia (Neale & Oltmanns, 1980), most twin researchers now acknowledge that register- or consecutive hospital admission-based twin studies obtain a less biased sample and find lower concordance rates than the older resident samples (see also Walker, Downey, & Caspi, 1991). Far from being rejected, Jackson's observations on this score have been used by twin researchers to improve their method.

4. *Contrary to genetic expectations, DZ twins were more concordant than siblings even though they have the same genetic relationship to each other.* Although some commentators (Kety & Matthyse, 1988; Plomin, DeFries, & McClearn, 1990) have claimed that there is no concordance rate difference between DZ twins and siblings, the DZ rate is higher in every schizophrenia twin study reporting both rates (Fischer, 1973; Gottesman & Shields, 1972; Kallmann, 1946; Kringlen,

<sup>1</sup>In the twin study literature the first member of a twin pair diagnosed with schizophrenia is often referred to as a "proband."

1967a; Slater, 1953) and is significantly higher in two studies (Fischer, 1973; Slater, 1953). Slater's figures are of particular interest. He discussed the concordance rate differences between his DZ twins and siblings as follows:

Of the binovular [DZ] schizophrenia pairs 14 per cent were concordant. The incidence of schizophrenia among the sibs of schizophrenics was only 5 per cent [26/568]; but the difference between the binovular twins and the sibs is probably attributable to the more thorough investigation of the former. (Slater, 1953, p. 86)

Slater's figure of 14% DZ concordance included 54 opposite-sex pairs.<sup>2</sup> If we look at his same-sex pairs the rate goes up to 18%, and for same-sex *female* DZs the rate is 22.5% (9/40; Slater, 1953, p. 35). According to the assumptions of the twin method there should be no difference between male and female or same-sex and opposite-sex DZ twins, and certainly not the astounding 5:1 concordance rate ratio between female DZs and siblings.

Several important twin researchers have acknowledged that DZ twins are more concordant than siblings. Gottesman (1991, p. 96) calculated the schizophrenia "risk factor" for a DZ twin of a person diagnosed with schizophrenia as 17%, whereas the non-twin sibling of a person diagnosed with schizophrenia has a risk factor of 9%. Others have recognized that the greater environmental similarity of twins contributes to their higher concordance rate. According to Shields (1968), a portion of the DZ/sibling concordance rate difference "might be due to the fact that twin partners are investigated more thoroughly than the sibs, and not entirely to the greater similarity of the environment of twins" (p. 98). And Kringlen (1976) concluded,

There is, in fact, a difference in concordance rates between DZ twins and ordinary siblings. . . . 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. (p. 431)

We see that Jackson's observation was confirmed by the data and by the opinions of several leading schizophrenia twin researchers. This leads us to the next comparison discussed by Jackson.

5. *Contrary to genetic expectations, female MZ twins (MZf) were more concordant than male MZ pairs (MZm).* Jackson argued that higher female concordance rates for schizophrenia, and by implication for other psychiatric diagnoses, were plausibly explained by environmental factors. In the following passage Jackson described how identification factors could affect twin concordance rates:

The heavy incidence of female pairs would point to there being a "closeness" in sisters, especially fraternal twin sisters, which might be accounted for, in part, by some of the following facts. Culturally, girls are more restricted in activities outside the

<sup>2</sup>All concordance rates discussed in this article use the "pairwise" concordance method, which is equal to the percentage of pairs who are concordant out of the total sample.

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home than are boys. This was especially true in the years nearer the Victorian era, the time at which the patients in these various studies were going through childhood and adolescence. . . . Under these conditions, the boys probably work away from home, whereas the girls help around the house or work as domestic servants, with little opportunities for social contacts. Close ties between sisters do not carry the opprobrium that they might with brothers. "Sissy" and "homosexual" implications would be more likely to attach to brothers than to sisters in our culture, especially in terms of kissing, hugging, handholding, and so on. . . . Sisters even more than brothers may experience considerable guilt and fear about establishing sexual relationships, and in turn would be driven back to each other as an outlet for feelings they dare not acknowledge. (Jackson, 1960, pp. 67-68)

Because male and female twin pairs have the same genetic relationship to each other, sex differences in schizophrenia concordance rates can be viewed as an indicator of the effects of environmental similarity and identity confusion on twin concordance rates. In making this claim, it should be emphasized that schizophrenia affects both sexes more or less equally (Gottesman, 1991; Rosenthal, 1970; Slater & Cowie, 1971). For this reason significant sex-based concordance rate differences can reflect only real differences, methodological error, or chance.

Gottesman and Shields (1982, p. 115) attempted to counter the claim that female MZ twins are more concordant for schizophrenia than male MZ twins by arguing that higher female MZ concordance can be explained by the method used to obtain twin subjects. They divided studies reporting concordance rates by sex into two categories:

- Those based on consecutive admissions to a psychiatric hospital or based on twin registers were labeled Group A and consisted of studies "based on consecutive admissions, twinship checked" (Essen-Möller, 1941; Fischer, 1973; Gottesman & Shields, 1972; Kringlen, 1967a; Slater's 1953 *consecutive* sample).

- Those based on the method of sampling resident psychiatric populations were labeled Group B and consisted of studies "not so based" (Inouye, 1961; Luxenberger, 1928; Rosanoff, Handy, Plesset, & Brush, 1934; Slater's 1953 *resident* sample).

Gottesman and Shields produced a table (1982, p. 115; first presented by Shields, 1968) showing that once the supposedly more biased resident samples are removed, concordance rate differences by sex are not statistically significant. Gottesman and Shields concluded from their reanalysis

There is no sex difference in concordance for schizophrenia and no difference in the representation in those samples with more complete and thorough sampling. The higher concordance in females is accounted for entirely by the use of samples with biases induced through the loss of certain cases. (1982, p. 114)

Before I comment on this claim, it should be noted that Gottesman and Shields (1976b, p. 448) stated elsewhere that even though "Female pairs are not significantly more concordant than males (MZ)" in spite of the fact that the pooled MZ

concordance rate (Group A + Group B) showed that female pairs were more concordant at the .019 probability level.

Gottesman and Shields did not provide a convincing argument for why cases based on registers or consecutive admissions should be separated from the resident-based samples.<sup>3</sup> Although studies based on registers and consecutive admissions might be less biased ways of obtaining twin pairs than the resident hospital method, all three methods are biased because they typically obtain subjects only from among those whose condition necessitated hospitalization.

As Gottesman and Shields correctly observed, both Kringlen and Fischer needed to use national psychiatric registers to obtain their subjects: "Their studies, therefore, are also hospital based" (Gottesman & Shields, 1976a, p. 372). Furthermore, Gottesman and Shields consistently defended the validity of twin studies that used the resident hospital sampling method (e.g., Kallmann, 1946), yet they found this method biased when attempting to explain why MZf pairs are consistently more concordant than MZm pairs.

It is puzzling that Gottesman and Shields would separate Slater's 1953 twin study into resident and consecutive samples for the purpose of eliminating the allegedly biased resident sample from the comparison. The breakdown of these two groups was first published by Gottesman and Shields in the mid-1960s (Gottesman & Shields, 1966a). Ironically, their discussion of the differences between Slater's two samples centered on the claim that there was little difference between them, as a way of defending the resident hospital method against earlier criticism by Rosenthal (1961).<sup>4</sup> The MZ concordance rates for the respective hospital-based samples were 65% for Slater's resident sample and 64% for Slater's consecutive admission sample (Gottesman & Shields, 1966a, p. 46).

Gottesman and Shields concluded that the "above internal analysis of Slater's material fails to show the hypothesized difference (Rosenthal, 1961) between resident population and consecutive admissions. . . . if there were a selective bias against concordant males, concordance in the resident sample when corrected for this bias would be higher" (Gottesman & Shields, 1966a, p. 46). As we have seen, they would later use the same distinction to argue for the *exclusion* of resident sample MZ twins from pooled sex-based concordance rate calculations on the grounds that these samples were biased against male concordance.

With the exception of Tienari (1963, 1975) and the NAS-NRC sample (Hoffer & Pollin, 1970), all schizophrenia twin studies have required hospital records in order to locate subjects. For this reason, the NAS-NRC and Tienari reports are the only studies warranting separate status in a table comparing differing concordance rates (although both studies looked at male twins only). It is also difficult to accept the qualitative distinction Gottesman and Shields drew between the

<sup>3</sup>Fourteen years earlier, Shields (1968, p. 107) had considered the resident samples "possibly less representative."

<sup>4</sup>In another paper, Gottesman and Shields (1966b, p. 815) argued that "The issue of sampling from the resident hospital versus consecutively is not as crucial as the type of hospital."

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different sampling methods when two paragraphs below their table they wrote, "We feel comfortable in concluding that the twin studies of schizophrenia as a whole represent variations on the same theme and are, in effect, sound replications of the same experiment," (1982, p. 115). Were they truly "sound replications of the same experiment" there would be no justification for excluding four resident hospital-based samples from tables comparing the pooled concordance rates for male and female MZ twins.

Incidentally, a re-calculation I have made of the figures from Gottesman and Shields' (1982) Group A produces a revised set of figures when it is based on a "strict" definition of schizophrenia. Using Fischer's (1973) strict definition and Essen-Möller's 0% 1941 strict MZ concordance rate (see Essen-Möller, 1970), the concordance rates for Gottesman and Shields's Group A are re-calculated as MZ female—23/61 (38%); MZ male—17/65 (26%),  $p = .093$ . Although this difference remains statistically nonsignificant, this is due primarily to the artificial splitting of the total MZ sample into two parts. Just as Gottesman and Shields had argued (1966a), there is no valid reason to separate the two samples.

Rosenthal (1970) also looked at the phenomenon of higher female concordance rates in the schizophrenia twin studies. In a discussion of sex-based differences in the six studies published through 1970 reporting rates for both sexes, he noted:

If we consider each sample of MZ or DZ twins as an independent test of the null hypothesis that there is no difference in concordance rates between male and female twins, we should expect that, by chance alone, the rate for males will be higher about half the time. We find instead that the female rate is higher in 12 out of 12 samples. It is difficult to say whether this finding is meaningful. (p. 123)

This finding is actually very meaningful, and Rosenthal thought so too in 1962 when he contributed a paper on the subject. In this (1962a) paper, Rosenthal demonstrated that concordance rates for schizophrenia were consistently and significantly higher for female twin pairs than for male pairs. By separately pooling male and female concordance rates in the four schizophrenia twin studies and providing a breakdown of their monozygotic twin pairs by sex, he was able to show that MZf pairs were significantly more concordant than MZm pairs (78.3% vs. 54.8%;  $\chi^2(1) = 5.328$ ,  $p = .02$ , Rosenthal, 1962a, pp. 402–403).<sup>5</sup> This finding would seem to support Jackson's argument, but Rosenthal (p. 414) offered three possible explanations:

- The findings may be artifacts produced by vagaries of sampling.
- The findings may be valid and explainable on a genetic basis.
- The findings may be valid and explainable on a psychological basis.

Although Rosenthal found problems with each of these explanations, he concluded, "it seems reasonable to infer that psychological factors are influenc-

<sup>5</sup>The headings "male" and "female" were accidentally transposed in Table 1 of that article.

ing the sex-concordance rates" (1962a, p. 420). The following passage illustrates how his belief that psychological factors influenced twin concordance rates was reconciled with the genetic theory of schizophrenia:

Even though the bodies of data presented have suggestive value in an accounting of the sex-concordance ratios found in studies of schizophrenia, the role of genetic factors cannot be excluded. However, if the found sex-concordance ratios are valid, it seems reasonable to conclude that some psychological factors are influencing these ratios in good part. (1962a, p. 419)

Rosenthal's article on the relationship between gender and twin concordance for schizophrenia was one of a series of papers widely cited by twin method supporters as contributing to several methodological improvements in twin research. Yet this article in fact lends support to one of Jackson's most important and devastating criticisms of the logic of the method itself.

An example of the confusion over the role of environmental effects on concordance rates is evidenced in the writings of James Shields, who was one of the most esteemed researchers of twins and a participant in two major schizophrenia twin studies. In a 1967 speech, Shields noted the evidence of environmental influences in the development of schizophrenia:

The best evidence of a statistical kind showing the importance of environmental factors in schizophrenia derived from family studies comes from three sets of findings: the higher incidence in DZ twins than in sibs, in same-sex sibs than in opposite-sex sibs and in female relatives than in males. In each case it is understandable that this should be so, though there are possible sources of bias, suggesting that some of the reported difference may be exaggerated. (Shields, 1968, p. 98)

Although Shields was discussing the results from family studies, he did not distinguish the utterly crucial difference between environmental effects on schizophrenia and environmental effects on familial or twin concordance. The finding of higher female rates in family and twin studies—but not in the general population—is suggestive of identification factors playing a major role in concordance, as is the higher rate found among same-sex siblings when compared with opposite-sex sibs, and DZ twins when compared with siblings. Shields was apparently unable to grasp the difference between the idea that environmental factors play a role in schizophrenia—which is acknowledged by all sides of the debate—and the role of environmental factors influencing concordance rates, which, if shown to exist, provide evidence in favor of the idea that the twin method is vulnerable to environmental confounds.

In general, leading twin researchers have either (a) acknowledged that female MZ pairs are more concordant than male MZs, (b) not discussed the issue, or (c) like Gottesman and Shields (1982), argued that the difference is the product of biased sampling methods.

6. *Contrary to genetic expectations, female DZ pairs (DZf) were more concordant than male DZ pairs (DZm).* Jackson noticed that female DZ twin pairs

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had a higher schizophrenia concordance rate in every study: "Like-sexed female fraternal twins have a significant and usually markedly increased concordance rate over like-sexed males" (Jackson, 1960, p. 67). For the most part, schizophrenia twin researchers have not responded to this observation. One researcher who did respond was Einar Kringlen (1967a). Like all schizophrenia twin researchers, he acknowledged that "the basic underlying assumption of the twin method is, of course, that environmental conditions of monozygotic twins do not differ from those of dizygotic twins" (p. 20). Later in his report Kringlen took up the question of higher concordance rates among female DZ pairs, admitting that "it is difficult to explain this tendency" (p. 91). He then offered Jackson's 1960 theory as a possible explanation for higher rates among female DZ pairs, adding

With an increasing female emancipation this sex difference in upbringing and attitudes toward boys and girls has diminished. This could offer an explanation of the disappearance of the higher female concordance rates in more recent studies. This phenomenon might also be related to national culture. One would then expect higher female concordance to be particularly pronounced in cultures where girls and women are most restricted in their activities, whereas the phenomenon would vanish in cultures where females enjoy equal rights with males. (Kringlen, 1967a, pp. 91-92)

If true, Kringlen's speculation would constitute a serious problem for twin method theory because the twin method cannot recognize that female DZ twins could be more concordant for environmental or social reasons. If this is acknowledged, environmental factors could completely explain the MZ/DZ concordance rate difference as well. The twin method could be measuring nothing more than the degree of psychological closeness and environmental similarity distinguishing MZ from DZ twin pairs.

Since the publication of Jackson's critique, several schizophrenia twin studies reported rates for male and female DZ twins, with mixed results, but Jackson's observation has not been seriously challenged by twin researchers.

7. *Contrary to genetic expectations, same-sex DZ twins (DZss) were more concordant than opposite-sex DZs (DZos).* As we have seen, the twin method specifically compares monozygotic twin pairs with same-sex dizygotic twins. However, several schizophrenia twin researchers collected concordance rate data for opposite-sex DZ pairs as well. These data provide another important method of testing one of the key assumptions of the twin method. Jackson posed the question quite well:

Obviously same-sexed and different-sexed fraternal twins have the genotypical relationship of ordinary siblings. Therefore, because it is not claimed that schizophrenia is a sex-linked disorder, one would not expect a difference in concordance for schizophrenia on a hereditary basis. On the other hand, if the hypothesis is correct that identical twins are more concordant for schizophrenia because of their "twinness," one would expect a higher incidence of concordance for schizophrenia in same-sexed fraternal twins because they are more alike from the identity standpoint than different-sexed fraternal twins. (1960, pp. 64-65)

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The pooled figures for schizophrenia twin studies reporting concordance rates for both types of DZ twins are  $DZ_{ss} = 59/523$ , or 11.3%, and  $DZ_{os} = 20/422$ , or 4.7% (Joseph, 1999b), meaning that the  $DZ_{ss}$  rate is more than double the  $DZ_{os}$  rate. This finding is consistent with the theory that twin identification is largely responsible for the differing rates.

In a study of 90 pairs of 6-year-old twins from the Chicago area (including 36  $DZ_{ss}$  and 19  $DZ_{os}$  pairs), Koch (1966, p. 234) asked individual twins to answer yes or no to the question of whether they desired to be like their sibling. Among the same-sex DZ twins, 57% answered "yes," whereas only 16% of the DZ opposite-sex twins answered this way. Although these twins were quite young, Koch's study went straight to the question of how much each twin identified with his or her co-twin.

Proponents of the twin method have not satisfactorily explained the fact that the pooled concordance rate for  $DZ_{ss}$  twins is more than double the rate for  $DZ_{os}$  twins. Typically, the difference is either acknowledged, denied, or ignored; rarely is an attempt made to offer a genetic explanation for the difference. Keefe and Harvey (1994) wrote that environmental differences between MZ and DZ twins are unlikely factors in concordance rate differences because "same-sex and opposite sex fraternal twins have exactly the same concordance rate for schizophrenia" (pp. 82–83), whereas Plomin et al. (1990) recognized that "opposite-sex twins have a consistently lower concordance" (p. 339).

Like Keefe and Harvey (1994), Gottesman and Shields (1982) denied that there are any differences between  $DZ_{os}$  and  $DZ_{ss}$  concordance rates, claiming "that opposite-sex twins, when studied, are no *less* concordant than same-sex fraternal twin-pairs . . ." (p. 114). They qualified this statement toward the end of their book, writing that "opposite-sex DZ pairs are as concordant as same-sex DZ pairs in recent studies" (p. 243). By referring to "recent studies," they created the impression of a trend while obscuring the fact that significant differences were found in the older investigations. In fact, the "recent studies" they were referring to was actually one study (Kringlen, 1967a).

In an earlier work, Gottesman and Shields had a much different analysis of the  $DZ_{ss}/DZ_{os}$  concordance rate difference: "One significant and consistent difference that emerged from our analyses was a lower concordance rate for opposite-sex fraternal pairs than same-sex fraternal pairs for studies giving information on this point" (1966a, p. 76). There was only one study reporting  $DZ_{ss}/DZ_{os}$  concordance rates in the intervening years, and it is therefore puzzling how Gottesman and Shields could have come to such different conclusions in 1966 and 1982 on the basis of very similar numbers.

At the pivotal 1967 Dorado Beach, Puerto Rico, schizophrenia conference, Shields observed:

The pooled crude concordance rates in six studies of 430 DZ pairs of opposite sex is only 5-6%, which is about half the concordance rate usually reported in DZ pairs of the same sex, and the difference is consistent in all studies except Kringlen's. (1968, p. 98)

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<sup>6</sup>In Rosenthal's (1966a) study of  $DZ_{ss}$  and  $DZ_{os}$  concordance rates, the difference was not significant (1966a, p. 98). Rosenthal (1966a) also presented evidence for the difference in concordance rates between  $DZ_{ss}$  and  $DZ_{os}$  twins.

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In this report, Shields saw Kringlen's (1967a) finding as the exception that proved the rule; it would only be in later years that this exception would become, in the minds of Gottesman and Shields, a "trend." And for the record, Kringlen's results were due to an unusually low DZss rate. His DZos rate is about the same as the pooled rate, whereas the DZss rate stands out from the others. In fact, Kringlen's DZss twins are significantly less concordant than the pooled DZss rate of the other five studies (3/69 or 4.3% vs. 56/454 or 12.3%,  $p = .03$ , Fisher's exact test, one-tailed; see Joseph, 1999b, Table 2). Gottesman and Shields' (1982) claim is also striking when one considers that these authors were the leading defenders of the studies of Kallmann (1946) and Slater (1953), whose figures showed statistically significant concordance rate differences between these two types of DZ twin pairs.<sup>6</sup>

In another report, Gottesman and Shields compared the findings of Kringlen's study to those of Kallmann:

Kringlen's overall pattern of results is impressively like that of Kallmann's: there were no significant sibling-DZ, male-female, or same-sex DZ/opposite-sex DZ differences in concordance rates, all three "nulls" leading to an emphasis on autosomal genetic factors and a deemphasis on sex role and identification factors. (Gottesman & Shields, 1976a, p. 373)

In fact, Kallmann's (1946) DZss twins *were* significantly more concordant than his DZos pairs, DZss = 34/296 (11%) vs. DZos = 13/221 (6%),  $p = .019$ , Fisher's exact test, one-tailed. Gottesman and Shields also overlooked the statistically significant differences between Slater's DZ twin/sibling and DZss/DZos samples, and the significant differences found in Fischer's (1973) DZ twin/sibling comparison.

In Gottesman's (1991) review of the schizophrenia twin study literature, his only mention of the DZss/DZos concordance rate difference was in the discussion of the Kringlen (1967a) finding of a higher rate in the DZos group: "[Kringlen] used males and females and studied opposite-sex as well as same-sex fraternal twins in extensive fieldwork, reporting no difference in these fraternal concordance rates with respect to schizophrenia" (p. 111). About the significant differences found in the studies of Slater and Kallmann, Gottesman said nothing.

Like the DZ/sibling, MZf/MZm, and DZf/DZm comparisons, Jackson's observation on the DZss/DZos concordance rate difference stands up to the responses of twin researchers.

8. *Individual case histories of reared-apart MZ twins concordant for schizophrenia do not provide important evidence for genetic factors because they were few in number (two), and the pairs grew up in similar environments and had an*

<sup>6</sup>In Rosenthal's (1962a) report the statistically significant difference between Kallmann's (1946) DZss and DZos pairs was presented in a table, to emphasize the point. Gottesman and Shields (1966a) also presented Kallmann's DZss-DZos totals in a table without calculating a probability figure for the difference.

*interactive relationship with each other.* Although several single-case histories have been reported in the literature since the publication of Jackson's paper, his main argument holds true today. Studies of reared-apart twins (using case studies or systematic ascertainment) suffer from several methodological problems such as investigator bias, the fact that twins often spent a considerable amount of time together and knew of each other's existence, sample bias, and the environmental similarity of reared-apart twins (see Farber, 1981; Joseph, 1999b, in press-b; Kamin, 1974). Even Gottesman (1991, p. 121) acknowledged that individual cases of reared-apart twins concordant for schizophrenia are of questionable scientific value and represent little more than "fascinating curiosities." As in 1960, the argument that twin studies support the genetic position is based primarily on reared-together MZ and DZ twins.

9. *Monozygotic twins grow up in a more similar environment and are treated more similarly than dizygotic twins. Therefore, greater MZ similarity or concordance could be explained by the more similar environment they experience.* Most modern twin researchers have conceded the point that monozygotic twins are treated more similarly and experience a more similar environment than dizygotics (e.g., Bouchard, 1993; Gottesman & Shields, 1972; Kendler, 1983; Kendler, Neale, Kessler, Heath, & Eaves, 1994; Rose, 1991; Scarr, 1968; Scarr & Carter-Saltzman, 1979), although several have argued that greater environmental similarity does not make MZ twins more similar. As documented elsewhere (Joseph, 1998b), the most important twin researchers of the 1960s agreed with Jackson that greater environmental similarity does increase MZ schizophrenia concordance rates. A few examples are cited here.

According to Essen-Möller (1963), one of the most respected schizophrenia twin researchers of his era, "Quite obviously, then, the logical evidence furnished by the classical twin method is not unambiguous, as originally believed. A greater concordance in monozygotics must not invariably depend on their genetic identity, since also their environment may have been more similar" (p. 69). In 1963, Tienari wrote, "It is apparent that differences in concordance rates between groups of identical and fraternal twins, as well as between female and male pairs, are partly attributable to environmental (psychological) effects" (pp. 120-121). According to Shields:

It is established that the MZ co-twins of schizophrenics are at least twice as often and, in many types of samples, 4 or 5 times as often schizophrenic as DZ co-twins of the same sex. This difference will be accounted for by influences from two sources: by the effects of the greater genetic similarity of MZ twins, and by greater similarity in environmental factors relevant to schizophrenia shared by MZ twins and not by DZ twins. (1968, p. 100)

And Kringlen, the investigator or co-investigator of two schizophrenia twin studies, concluded that

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

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Thus, most schizophrenia twin researchers conceded Jackson's point about the greater environmental similarity of MZ twins, and several acknowledged that this similarity has affected concordance rates. Of course, no twin researcher has claimed that environmental similarity explains the entire MZ/DZ concordance rate difference, which would mean nothing less than the acknowledgment that the twin method is useless as an instrument for detecting genetic influences on psychological trait differences.

10. *Contrary to the genetic hypothesis, the psychodynamic thesis predicts that concordance rates should correlate with the degree of likeness among siblings, regardless of their genetic relationship.* This argument finds support in the schizophrenia twin data that show that twin and non-twin sibling concordance for schizophrenia is correlated with environmental similarity and psychological association (for twin data, see Kringlen, 1967a, p. 115, Table 46). Twin researchers have supplied quantitative data that they claim support the idea that environmental or treatment similarity does not produce behavioral similarity (e.g., Kendler, Neale, Kessler, Heath, & Eaves, 1992; Loehlin & Nichols, 1976; Morris-Yates, Andrews, Howie, & Henderson, 1990). However, these claims do not hold up to critical analysis (see Joseph, 1998a, 1998b; Pam, Kemker, Ross, & Golden, 1996).

It is noteworthy that most twin researchers would not hesitate to acknowledge that *family studies* are confounded by the fact that families share a common environment as well as common genes but do not extend this observation to MZ/DZ comparisons in spite of their understanding that MZ twins share a more correlated environment as well as a greater genetic similarity (Joseph, 2000a, 2000b).

11. *The unique psychological bond or "ego fusion" of MZ twins contributes to a higher MZ concordance rate for schizophrenia on the basis of association and identification. Furthermore, the identical twinship itself might create conditions leading to the identity problems often experienced by people diagnosed with schizophrenia.* This is the most discussed of Jackson's major contentions and therefore requires a detailed examination.

Jackson saw the unique psychological bond of identical twins not only as explaining high schizophrenia concordance rates but also as an additional *cause* of "madness." On the occasions that defenders of the twin method have directly addressed Jackson's ideas, this is the charge that is most often made against him. Let us examine the citations in question. According to Jackson (1960):

The identity problems of the schizophrenic, most often stressed by psychodynamically oriented writers, could find no better nidus than in the intertwining of twin identities, in the ego fusion that in one sense doubles the ego (because the other is felt as part of the self) and in another sense halves it (because the self is felt as part of the other). (p. 66)

If the psychodynamic thesis is correct, if ego fusion in a particular family environment can be expected to lead to joint madness, then a plausible hypothesis—contrary

to the genetical hypothesis—would be that, according to the degree of likeness in siblings, we will find an increased concordance for schizophrenia, without concern for genetic similarity. (p. 67)

Psychosis by association apparently requires the nidus of social isolation for its hatching. . . . These characteristics increase the separation of the twin-pair from the rest of the world and foster a joint ego fusion. . . . The attempt of one to be like the other is not dissimilar to the ego fusion of some twins. (p. 69)

Here Jackson discusses how the intimate bond and “ego fusion” experienced by identical twins might weaken or blur the psychological boundaries between them. Although the implication (in the phrase “no better nidus”) that an individual MZ twin might be more susceptible to schizophrenia than a single-born individual is open to question, Jackson’s concept of ego fusion is an excellent description of psychodynamic factors that could induce one’s twin to become psychotic much more frequently than one’s non-twin sibling.

Against the idea that the close psychological association of MZ pairs leads to higher concordance rates, Gottesman and Shields (1972, p. 26) countered with the claim that “some pairs only become concordant after a lapse of two or three decades.” But in a later report Gottesman (1991) would conclude, “It has been observed that identical twins who are going to become concordant for schizophrenia do so within three to five years after the first twin falls ill” (p. 108). This observation only strengthens Jackson’s original argument.

The most serious attempt to counter Jackson’s ideas was made by David Rosenthal, whose 1960 article has been widely cited by twin researchers as the definitive answer to Jackson’s argument. Rosenthal addressed the theory that “persons who develop ‘confusion of ego identity’ are said to be especially vulnerable to schizophrenia. . . . Jackson has been an articulate advocate of this idea” (p. 297). Rosenthal cited evidence from twin studies which, he claimed, showed that twins do not develop schizophrenia at rates significantly higher than the single-born population.<sup>7</sup> However, a recent study based on the New Danish Twin Register (Klänning, Mortensen, & Kyvik, 1996) found that twins had a 28% higher rate of first admission for schizophrenia when compared with the general population ( $p = .002$ ).

Thus, the question remains open. More important is that the inconclusive evidence in support of the idea that MZ twins are more vulnerable to schizophrenia does not detract from Jackson’s basic argument because his “confusion of ego identity theory” does not require that MZ twins develop schizophrenia at rates greater than the single-born population. Jackson argued that the confusion of ego identity, experienced most strongly by identical twins, could explain why the co-twin of a schizophrenic would be more likely to become schizophrenic than an

<sup>7</sup>Although Tienari (1963, p. 120) concluded from his own investigation into this question that “the results would appear to speak against Rosenthal’s assumption, rather than to support it,” Kringlen’s study (1967a) provided support for Rosenthal’s findings.

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Jackson's hypothesis has been cited by several twin researchers as proof that his entire argument was faulty, thus becoming a sort of "straw man" in the case against Jackson. Kringlen's position is typical:

The findings furthermore cast doubt on Jackson's (1960) 'confusion of ego identity theory' of schizophrenia. . . . According to Jackson, the monozygotic twinship involves problems of 'isolation, association and identification.' This hypothesis stimulated Rosenthal (1960) to investigate if schizophrenia in fact was more frequent in twins. . . . Rosenthal analyzed the twin investigations published by Luxenberger . . . and Essen-Möller and could not support this theory of Jackson. (1967a, p. 61)

Like other critics, Kringlen falsely claimed that the "confusion of ego identity theory" must fall if identical twins are not more susceptible to schizophrenia than are members of the single-born population. However, as even Rosenthal acknowledged (see the next quotation), the identification hypothesis, if true, would not imply "a higher rate of illness in MZ twins" (although Rosenthal did make other statements contradicting this passage). And as we will see, a read-through of Kringlen's case histories clearly demonstrates the "isolation, association, and identification" of several of his concordant MZ pairs.

Rosenthal went on to concede that the rest of Jackson's ego fusion hypothesis may have been correct. To the question of whether the closer psychological identity of twins in general, and of MZ twins in particular, could have any effect on twin concordance rates, Rosenthal reasoned as follows:

The above findings do not rule out the possibility of other psychological hypotheses which might account for higher familial incidence, higher concordance in MZ than DZ twins, and no higher frequency of the illness in twins than in nontwins. *An hypothesis like "identification" might account for the higher concordance rate of illness in MZ twins without implying a higher rate of illness in MZ twins* [italics added] . . . . One could imagine a co-twin being drawn toward schizophrenic behavior if his twin had become schizophrenic and if he felt himself to be so much like his twin that he was completely convinced that the fate which had befallen his twin would befall him as well. He might be unable to resist this conviction, and presumably could behave in accordance with it. (1960, p. 303)

Jackson could not have said it any better himself.

By acknowledging the possibility that the closer psychological identification of MZ twins could lead to higher concordance rates (just as we have seen him concede that female twin pairs may be more concordant for schizophrenia due to closer association), Rosenthal undermined a critical assumption of the twin method. He had accused Jackson of casting doubt on the idea that "the environments of MZ and DZ twins are essentially equal" (Rosenthal, 1960, p. 298) and added that according to Jackson, "having an identical twin makes the environment of MZ twins unique" (p. 298). But we have just seen Rosenthal himself describe the real possibility of just such a "unique environment." And in an appar-

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ent departure from the medical model of schizophrenia, Rosenthal characterized schizophrenia as a "behavior" that one could be "drawn toward" rather than a disease of the central nervous system.

In the process of answering one relatively unimportant argument of Jackson's, Rosenthal conceded the plausibility of the idea that environmental theorists have maintained from the beginning that the psychological bond between MZ twins is a unique phenomenon that contributes to—or explains entirely—their greater similarity when compared with DZ twins.

Another prominent schizophrenia researcher observed that the larger studies found a 15% DZ concordance rate and that

It has . . . been claimed that if one limits the studies of dizygotic twins to same sexed pairs, preferably female, the concordance rate is higher than 15 per cent (Jackson, 1960). The data do not support this contention. Kallmann (1946) reported a risk of 17 per cent in same sexed dizygotic twins, and the risk was equal for males and females. Essen-Möller (1963) derived a rate of 13 per cent in the pooled world data on same sexed dizygotic twins. The basic premise seems faulty, that the over-all group, which shows no increase over that in sibs, could contain a large subgroup with a higher risk, while there seems no reason to postulate that another group would have a lower risk. An increase in one subgroup should raise the total figure. (Karlsson, 1966, pp. 20–21)

Slater's (1953) previously discussed figures contradict Karlsson's (1966) claim that DZ twins are no more concordant than ordinary siblings. Karlsson is one of the few commentators to cite Kallmann's 1946 figures on sex differences between DZf and DZm pairs, because Kallmann did not report how many pairs in each group were concordant for schizophrenia. Thus Kallmann's "morbidity" estimates are possibly useful in determining which group had a higher rate but not in the determination of the rate itself. Karlsson claimed that the "basic premise" of a higher concordance rate among DZ female pairs is "faulty," but every schizophrenia twin study through 1965 had reported higher DZ female rates.

Karlsson (1966) also claimed that Jackson compared DZ female rates with the *pooled* DZ rate when in fact he compared rates between DZ females and DZ males, as the female rate is a component of the pooled rate. Karlsson also failed to mention the significant differences between DZ same-sex and DZ opposite-sex pairs found in the reports of Kallmann (1946) and Slater (1953) or the importance of this finding as discussed by Jackson and Rosenthal. He cited Essen-Möller's (1963) pooled DZ same-sex concordance rate of 13%, while failing to mention that the pooled *opposite-sex* rate was 5–6%. No genetic theory can account for this difference.

Neale and Oltmanns (1980), the authors of a textbook on schizophrenia and strong supporters of the twin method and of the conclusions of schizophrenia twin studies, approached Jackson's argument from another direction:

Jackson . . . argued that the MZ/DZ comparison might not hold environmental factors constant, as had been assumed. He cited evidence that MZ twins tend to be more often dressed alike, less often separated, and so on. Nevertheless, as we have dis-

cussed before, regular sibling MZ and DZ concordance rates are not significantly different from each other, and the environmental factors are not constant.

Like Karlsson, Jackson's basic argument for schizophrenia is that the very phenomenon of schizophrenia is an environmental effect, not a genetic one, for non-twin siblings.

Second, N. Slater (1953) argued that the difference between MZ and DZ twins is not due to genetic factors. However, Slater's argument is based on the fact that fraternal twins' concordance rates are lower than MZ twins' simply that MZ twins share a level of ego function that fraternal twins do not. Slater and Oltmanns' argument that environmental factors "must be constant" in DZ twins is not convincing.

Neale and Oltmanns' method "that both MZ and DZ twins are addressed several times in the same leagues and are not that these investigators have investigated the difference is possible.

As we have seen, the environmental factors are not constant between MZ and DZ twins (p. 431), and Pollock also environmental factors, different groups, different well as by genetic factors and Oltmanns' argument "constant" with the environment or co-authors of the book.

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cussed before, MZ and DZ twins' environments must be more similar than those of regular siblings. And the difference in concordance rates is much greater between MZ and DZ twins than between DZ twins and normal siblings. Thus factors other than environment must be operating. (p. 183)

Like Karlsson, Neale and Oltmanns (1980) did not make inroads against Jackson's basic argument. First, by admitting that DZ twins are more concordant for schizophrenia than normal siblings, Neale and Oltmanns acknowledged the very phenomenon they were attempting to refute, namely, that the more similar environment experienced by twins produces higher concordance rates than rates for non-twin siblings, whose genetic relationship is the same as DZ twins.

Second, Neale and Oltmanns (1980) assume that environmental differences between MZ and DZ twins are more similar than between DZ twins and ordinary siblings. However, it is quite possible that the difference between identical and fraternal twins' psychological bond and similarity of treatment is far greater than between fraternal twins and siblings. The thrust of Jackson's argument was not simply that MZ twins share a more similar environment but that they experience a level of ego fusion unmatched by any other type of human relationship. Neale and Oltmanns' false premise leads to the equally false conclusion that genetic factors "must be operating" in MZ/DZ comparisons. Their DZ twin/sibling discussion, however, leads to the conclusion that environmental factors must be operating in DZ twin concordance rates.

Neale and Oltmanns (1980) endorsed the basic assumption of the twin method "that both forms of twins share very similar environments" (p. 168) and addressed several other implications of Jackson's critique, citing Pollin and colleagues and an early paper by Kringlen (1964) in their defense. It is interesting that these investigators were mentioned in this discussion because Pollin and Kringlen have acknowledged that the MZ/DZ schizophrenia concordance rate difference is partly attributable to environmental influences.

As we have seen, to the question of whether the twin method "holds environmental factors constant," Kringlen wrote, "The total difference in concordance rates between MZ and DZ twins cannot be ascribed to genetic factors only" (1976, p. 431), and Pollin (with Hoffer) asserted, "Because there are not only genetic but also environmental differences between the monozygotic group and the dizygotic group, differences in concordance rates may be explained by environmental as well as by genetic hypotheses" (Hoffer & Pollin, 1970, p. 476). How can Neale and Oltmanns reconcile their assertion that environmental factors are "held constant" with the statements of these researchers, who were themselves the authors or co-authors of 3 of the 14 schizophrenia twin studies?

The case histories of concordant monozygotic twins provide support to Jackson's thesis that the close association of identical twins plays a major role in concordance. Selected passages from relevant case histories will be examined. Whether the pairs in question should have been considered concordant for schizophrenia is not our concern at the moment. What is important is the nature of the

relationship between the twins. We will look at case histories recorded both before and after Jackson's 1960 critique. One should keep in mind that most of these histories were written by people with little interest in psychodynamic processes, and it is therefore likely that they failed to adequately capture the essence of the bond between the twins.

Rosanoff et al. (1934, pp. 257–258) provided a sketch of identical twins, George and Foster, whom they counted as concordant for schizophrenia “but in a manner quantitatively dissimilar.” The twins were born in Ohio in 1906. George was committed to a mental hospital in June of 1930 and received a diagnosis of dementia praecox (schizophrenia). According to the case history, “The twins had always been together and had always been devoted to each other. When George was taken to the hospital Foster began to worry greatly. . . . He lost all ambition to work, sat around at home ‘just thinking,’ [and] paid no attention to any one who spoke to him.” Foster was finally convinced to seek voluntary admission to a mental hospital “for a couple of weeks’ rest and change,” but he would not remain long:

While he was there word came that George was better and could come home on a trial visit. “*The minute that Foster heard that, he snapped right out of it, brightened up, and the two boys came home the same day*” [italics added]. He resumed his work and seemed as well as ever. At the time of our observation of the case he appeared quite normal mentally. (Rosanoff et al., 1934, p. 258)

This is a touching story of an identical twin who felt so close to his co-twin that he was willing to follow him into a mental hospital. Upon hearing that his twin brother had been released from the hospital, Foster's “subacute schizophrenia” symptoms vanished almost immediately as he happily rejoined his twin brother in the family home.

The next English-language schizophrenia twin study to provide case histories was Slater's 1953 report, which was the last to be published before the appearance of Jackson's critique. Case history excerpts from some of the most interesting pairs of concordant MZ schizophrenic twins follow:

**Pair 20, females, born 1894.** (Lily and Mary). Following disagreements at home Lily and Mary left in 1914 to live together, and have done so since. The first signs of their deafness came on about then. They rather shut themselves up together, with little outside contact. . . . According to a neighbor, they were well known in the neighborhood for their likeness to one another. . . . Both have paranoid illnesses coming on at the time of the menopause and within 2 years of one another. (Slater, 1953, pp. 127–129)

**Pair 110, females, born 1872.** (Marjorie and Cynthia). Until they were 40 they lived at home. . . . Marjorie was the first to become peculiar. . . . Cynthia became ill very suddenly, about two years after Marjorie had begun to be peculiar. . . . Eventually they both barricaded the flat, which led to their certification and admission to [the mental hospital] on the same day in June, 1918, aged 46. (p. 150)

**Pair 198/199, females, born 1912.** (Irene and Maureen). They were always much alike, short and thin with dark eyes. And dark straight hair. They were frequently mis-

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taken for one another, and at one time one twin deputised for the other at the factory where she worked without anyone noticing. They always remained intimate and never troubled to make separate friends. Many 'telepathic' experiences are reported; if one fell down at one spot the other would too, and hurt the same knee. Maureen is said to have had pains when Irene had her baby. . . . At the present time both twins are attending a psychiatric clinic where observation has shown that in both symptoms are much worse just before the periods. . . . The first remark [in an interview], on being introduced by their mother, was: "Yes, we're the twins, and we're still ill. It's a mysterious illness, ours." They seemed to share one illness between them. (pp. 166-168)

**Pair 287, males, born 1915.** (Leslie and Reginald). In April 1940, [Leslie] was admitted to a general hospital. . . . Reggie attended the psychiatric clinic in 1940 with his twin, and he said that he himself had bad nerves, got into arguments, had few interests. . . . When Leslie was certified in 1940, Reggie was very upset and would say: "I've murdered my brother, I've poisoned him" . . . He wandered about at night picking at biscuits and would call his parents names. . . . In April 1941 he became violent, attacked his parents and was taken to the observation ward and to the mental hospital. (pp. 175-176)

Kringlen (1967b) also provided case histories for his pairs. The following excerpts describe the isolation and association of several concordant MZ pairs. Twin pair members are referred to as *Twin A* and *Twin B*.

**Case 1, males, born 1913.** As children, they were mistaken for the other, even by their parents. . . . They were brought up alike, dressed in the same way, and were much together as children. . . . [Twin A] was transferred to a mental hospital [in 1934]. . . . [Twin] B had a short period of "nervousness" at age 19 when his brother became ill. . . . Then he seemed to have been all right until the age of 21, when his brother was admitted to the hospital. He visited his brother often, and said to his family after some time that he felt he himself had to go to the hospital. . . . Both twins were seen in 1965 in the same hospital where they have stayed. Both are living in the same room. (pp. 4-7)

**Case 2, males, born 1921.** Mistaken for each other as children by the teacher. Extremely strong attachment to each other. . . . Before the age of 25 they had been separated for only very short periods of time. . . . [Twin A] admitted to a mental hospital in 1947. . . . B became psychotic in 1949. (pp. 10-11)

**Case 3, males, born 1916.** They were always together as children, and made the same few friends. They were, however, living in an isolated area and consequently had slight contact with other children. If one was home from school because of illness, the other one also stayed home, even if he was not sick. . . . They were not separated until they were 20 years old. . . . [Twin A at age 30] was living with his twin brother on the isolated family farm up in the hills and they had practically no contact with other people. . . . [Twin] A was placed in a mental hospital 1957-1958. . . . [Also in 1957, Twin B] began being more overly disturbed, knocking at the walls, scolding into the air, apparently hallucinated. [Admitted to a mental hospital, 1959]. (pp. 15-19)

**Case 4, males, born 1930.** As children the twins were mistaken for one another by their teachers, and considered as alike as two drops of water. . . . They were inseparable as children, and even more so as adults. . . . They were never separated from one another. . . . [Twin A was admitted to a mental hospital in 1949]. At admittance

he was accompanied by his parents and his twin brother. . . . [Twin] B was attending a technical school when his brother got sick. Some time afterwards he lost interest in the school work, started sleeping poorly and stayed up at night. . . . [Twin B hospitalized in 1951]. (pp. 22–25)

**Case 5, males, born 1909.** [Mother] did not allow the children to bring friends home with them—did not like them to mix too much with others. . . . (p. 29)

**Case 6, males, born 1908.** As children, their siblings could not tell them apart—they were like two drops of water. They had only slight contact with the other children and clung together most of the time. Their attachment was extremely strong in childhood and even after puberty. They were never separated before the age of 17. (p. 34)

**Case 9, females, born 1907.** They always clung together, and were extremely dependent on one another also as adults. They seemed to have “normal” contact with other children, but they never made separate companions among their friends. . . . [Twin A] started getting ill when she was 39 years old. . . . When [Twin] A was hospitalized in 1952, [Twin] B stayed home with marginal social functioning. She was longing intensely for her sister’s company. . . . [In 1959, after being placed in a sanitarium, Twin B] was soon transferred to the same mental hospital in which her twin sister was (1959) and has since stayed there together with [Twin] A. . . . Both twins were seen in the hospital in 1965. They came to my office dressed in the same way, walking and behaving in much the same way—a remarkable couple. The nurses told me that the twins were together all day long. (pp. 48–53)

**Case 10, females, born 1930.** As children, they were greatly dependent on each other and virtually inseparable. . . . [Twin A’s] first hospitalization period was from December 1953, to April 1954. . . . When [Twin] A was hospitalized, [Twin] B said: “Why don’t they take me, too”. . . . [Twin] B became psychotic when she was 25 years old. (pp. 56–58)

**Case 12, females, born 1923.** The twins grew up on a small, lonely farm. . . . Neither twin went about with other girls or boys much. . . . At the age of 22–23, Twin A developed a catatonic-like remittent schizophrenia. . . . [Twin] B began to be “nervous” when [Twin] A was admitted to the hospital in 1944. . . . Twin B fell ill shortly after [Twin] A, with approximately the same symptoms. (pp. 65–69)

Like the Rosanoff et al. (1934) George and Foster case, several of Kringlen’s twins were apparently so distraught over the hospitalization of their co-twin that they were willing to follow him or her into a mental hospital in order to continue the relationship. In Case 10, when Twin A was being taken to a mental hospital her identical twin sister cried out, “Why don’t they take me, too?” A more compelling (though tragic) human drama could hardly be imagined.

The following notes are excerpted from the case histories of concordant monozygotic twins studied by Gottesman and Shields (1972):

**Pair 1, males, born 1893.** (Twins A and B both diagnosed with schizophrenia at age 30).

[Mother] idolized twins, gave them most similar names she could think of; overprotected them in that she did not allow them to mix with other children. . . . The twins were inseparable until 18 years of age. . . . Taken in isolation this pair should *not* give more comfort to genetic enthusiasts than to environmental ones with respect to

weighting the influence of symptoms. (

**Pair 7, females, born 1893.** Twin B diagnosed

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**Pair 17, males, born 1893.** Twin B diagnosed age 22. The twin

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symptoms. (pp. 72–75)

**Pair 7, females, born 1940.** (Twin A diagnosed with schizophrenia at age  
18, Twin B diagnosed with schizophrenia at age 19).

Twins very close—"couldn't make a move without the other." They had few friends  
. . . [The twins] were extremely dependent on their [mother] who encouraged their  
dependence. . . . *Psychiatric history of B.* Behavior gradually became unpredictable  
and irrational after transfer to another library and [Twin] A became ill (at 17); ac-  
cused [mother] of causing twin's illness . . . later increasingly withdrawn. . . . This  
East End London family parallels those described in the psychodynamic family study  
literature of Lidz and others. (pp. 88–91)

**Pair 17, males, born 1934.** (Both twins were diagnosed as schizophrenic at  
age 22. The twins were separated at birth but lived together for 1 year at age 5).

The arrival, for the first time since his adoption, of the biological mother at A's home  
early in October preceded his manifestly odd behavior by about 2 months. B was  
taken to visit his sick twin on December 22 in the belief that this might improve A's  
condition. Instead it appears to have precipitated B's illness, for the same evening he  
was disturbed and on January 5 was admitted to hospital, just before A. (pp.  
114–118)

**Pair 19, females, born 1926.** (Twin A diagnosed with schizophrenia at age  
31, Twin B diagnosed with schizophrenia at age 35).

Both stubborn children; later, as adolescents, backward "but nice"; regarded as  
moody, suspicious, "keeping together". . . . Both remained single. . . . [Twin B had  
no symptoms until she] joined "wild scene" when A became disturbed (onset): felt  
persecuted, thought food poisoned, tried to jump through window; became equally  
disturbed as A and talked about attempts to murder A. Together admitted to observa-  
tion ward (at 31) where wept and wailed continuously. . . . Socialized only with twin,  
upset by any suggestion of separation, once responded immediately by breaking  
vase. . . . It is reasonable to raise questions of folie à deux and culture shock in this  
pair. Clearly their twinship was responsible for their shared delusions and simulta-  
neous onset of psychosis. (pp. 122–124)

These descriptions are consistent with Jackson's observation that isolation,  
association, and identity confusion are common themes among concordant MZ  
twin pairs. Throughout these case histories, we encounter observations such as  
"they rather shut themselves up together," "never troubled to make separate  
friends," "no contact with other people," "they seemed to share one illness be-  
tween them," "were never separated from one another," "longing intensely for  
her sister's company," "did not like to mix too much with others," "always clung  
together," "inseparable," "couldn't make a move without the other," and so on. To  
be sure, there have been pairs closely associated in isolation who were discordant  
for schizophrenia. The point is only that these conditions are associated with  
higher concordance rates found among identical twins.

To summarize, twin method proponents have attempted to dismiss Jackson's

entire argument by claiming that the evidence does not support his suggestion that identical twins might be more susceptible to schizophrenia than members of the single-born population. Although there is inconclusive evidence in favor of his suggestion, it is not central to Jackson's argument. At the heart of Jackson's theory lies a psychodynamic explanation of why a twin follows his or her co-twin into psychosis—not why the first member of a pair becomes schizophrenic.

12. *There is a striking similarity between reports of folie à deux (shared psychotic disorder) and the case histories of MZ twins concordant for schizophrenia.* Cases of folie à deux, or shared psychotic disorder, have been reported in the literature since the 19th century. Folie à deux has been defined as "a psychiatric entity characterized by the transference of delusional ideas and/or abnormal behavior from one person to one or more others who have been in close association with the primarily affected person" (Gralnick, 1942, p. 232). A comparison of this concept and concordance for schizophrenia among identical twins made up the final section of Jackson's critique.

Jackson noted that long-standing association and social isolation were common factors linking folie à deux and the case histories of concordant MZ twins. He stressed that the association was not necessarily a positive one but that "every twin report I have discussed mentions the strength of attachment between the pair, either in positive terms or in terms of mutual antagonism and jealousy. There are no indifferent cases" (1960, p. 68). Jackson noted that, in Kallmann's (1946) twin study, MZ twins (average age, 33 years) who had lived apart for 5 years or more were listed as having a 77.6% concordance rate, whereas "non-separated" pairs were listed as having a 91.5% concordance rate. Thus, "a separation even past the formative years was apparently very effective in reducing the concordance rate" (Jackson, 1960, p. 69).

Jackson also observed that, like concordant pairs from the schizophrenia twin studies, folie à deux was much more common among female pairs. According to Gralnick's (1942) review of the English language reports on folie à deux, case histories fell into the following patterns: sisters involved (40 cases), brothers involved (11 cases), brothers and sisters involved (6 cases); mother-child (24 cases), father-child (2 cases); husband and wife (26 cases); nonconsanguineous (9 cases).

Although there are obvious limitations in comparing case history totals, these figures are consistent with the greater rate of shared psychosis found among female family members and female twins. For Gralnick, the fact that many pairs in his review were blood relatives was not necessarily proof of the existence of a genetic component since it "is only within the family unit, as we know it, that all or most of the factors and mechanisms which have been cited can operate" (p. 245). One quarter of the case histories described husband and wife pairs, who in most cases are not blood relatives.

A paper from Japan (Kashiwase & Kato, 1997) reviewed all 97 case histo-

ries of folie à deux in the 67 cases involving couples, which combined with the 30 cases of folie à deux in Japan involving who simply shared combinations, but a rem-

The lack of familial closeness experienced at home. There was no concordance in 16% and 13% of pairs (16% and 13%); this is likely due to the fact that they were together outside the family. The statistics of counting concordant cases of folie à deux in Japan are correlated to levels of c-

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ries of folie à deux reported in the Japanese literature between 1904 and 1994. Of the 67 cases involving family members, the authors found that 30% were married couples, which cannot be explained on the basis of genetic similarity. When combined with the 30 non-familial cases, more than 50% of the reported cases of folie à deux in Japan involved people with no biological relationship to each other but who simply shared a close association. Another 34% involved parent-child combinations, but a remarkable 22 out of 23 such cases were mother-child pairs.

The lack of father-child pairs is best explained by the physical and emotional closeness experienced by a child and the parent spending more time in the home. There was surprisingly little difference between brother pairs and sister pairs (16% and 13%, respectively). Kashiwase and Kato (1997) explained that this is likely due to the fact that in Japan, sisters had much less opportunity to live together outside the home compared with sisters in Western countries. The limitations of counting case histories should again be noted, but the reports of folie à deux in Japan are consistent with the idea that high concordance for psychosis is related to levels of closeness and association.

Because one of the defining features of folie à deux is that the delusional ideas of the pair are similar, not all twin pairs concordant for schizophrenia could be placed in this category. Nevertheless, the concept speaks strongly to the idea that closely associated people can become psychotic for interpersonal reasons. Rioux (1963) provided a psychodynamic explanation of the interactions between the members of a pair, leading to folie à deux:

The submissive companion becomes anxious. He sees himself threatened with either the loss of his dependency relationship or the loss of reality. . . . He sees his companion, who is now his universe, proceeding into psychosis—alone if need be. More acutely than ever, he realizes the equation between breaking away from his deluded companion and starting a new life of initiative and independence. He does not know how to be independent; and, alone, it would be impossible to learn. But, continuing to accept the dominant partner even with his delusions—which after all are meaningful enough to encourage identification—is easier and more in keeping with his character and the way he is accustomed to live. Thus, the one-way of dependency in him creates the necessity of adopting the delusional system proposed by the inducer. Folie à deux saves the alliance: the symbiotic couple remains united but for worse, rather than for better. (pp. 410–411)

Nothing in Rioux's eloquent description implies that the association itself contributes to the delusional system of one member of the pair, but it does speak to the cause of the *second* member's delusional system. That is precisely the point that Jackson attempted to make. In the case of identical twins who see themselves as two halves of the same whole, the fall into psychosis of the submissive twin may not only be a way of saving the alliance but may well be perceived as the only way of *saving the self*. And it has already been noted in the cases of concordant MZ pairs that when one twin becomes schizophrenic, the other is usually diagnosed within 5 years—in spite of the fact that the "risk period" for schizophrenia is usually given as ages 15–45.

The *Diagnostic and Statistical Manual, Fourth Edition (DSM-IV)* (American Psychiatric Association, 1994, pp. 305–306) recognizes folie à deux (or Shared Psychotic Disorder) as a mental disorder, thereby acknowledging that a member of a closely associated pair can become psychotic on the basis of identification and association. Yet in the Familial Pattern section for schizophrenia (p. 283), the genetic basis of schizophrenia is supported (in part) by the finding that “Concordance rates for Schizophrenia are higher in monozygotic twins than in dizygotic twins.”

Because the finding of a genetic factor in schizophrenia twin studies depends on the assumption that degrees of twin closeness could not have played a role in increased MZ concordance rates, there is a conflict between the recognition of the concept of folie à deux and the citing of twin studies in support of the alleged genetic basis of schizophrenia. The *DSM-IV* recognizes that a member of a closely associated pair can become psychotic for reasons of the association but if the psychosis is labeled *schizophrenia*, then association could not have played a role (according to twin method assumptions). It is difficult to make sense of this.

As Jackson observed, “If twinness itself is an important contributor to the high concordance rate in identical twins, then one might expect clinical resemblances between their psychoses and folie à deux” (1960, p. 68). There is reason to believe that MZ concordance rates for schizophrenia, as well as virtually every other type of human behavior, are influenced by identification factors recognized in the folie à deux concept.

### Discussion

We have seen that not one of Jackson’s 12 major points was convincingly disproved by twin researchers, and many were acknowledged. In countless books and articles discussing (or rather, briefly dismissing) Jackson’s thesis we find the claim that Jackson’s argument does not hold up because it is alleged that twins are no more susceptible to schizophrenia than are members of the single-born population. Proponents of the twin method have used this argument in an attempt to invalidate Jackson’s most important observations.

However, Jackson’s most telling point was that among pairs with the same genetic relationship to each other, those pairs experiencing a more similar environment and closer emotional bond were consistently more concordant for schizophrenia. For Jackson, this suggested that the MZ/DZ concordance rate difference (already inflated by methodological bias) could be explained on environmental grounds.

In response to Jackson’s irresistible argument, Rosenthal authored a series of critical articles documenting the problems with the schizophrenia twin studies. In the main, this “constructive critic” of the twin method conceded Jackson’s most important points, yet continued to uphold the twin method as a valid instrument for the detection of genetic influences. It would only be in later years that Rosenthal would conclude that both consanguinity studies and the twin method were

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(*DSM-IV*; American Psychiatric Association, 1994) that a member of a pair of identical and fraternal twins (p. 283), the genetic etiology that "Concordance for schizophrenia in dizygotic twins." The validity of twin studies depends on the recognition of the nature of the alleged genetic contribution but if the environment played a role (accident) sense of this. The environment is not a contributor to the clinical resemblance (p. 68). There is reason to believe that as virtually every factor is recognized

as was convincingly demonstrated. In countless books on the subject of twins we find the claim that twins raised apart of the single-born environment in an attempt

to compare pairs with the same environment and a more similar environment. The concordance rate difference is explained on environ-

ment. The author of a series of papers on schizophrenia twin studies. In addition to Jackson's most recent work, a valid instrument for the past several years that Rosenhan's twin method were

"confounded," and that "one can draw conclusions about them only at considerable risk" (1979, p. 25).

We have seen how other twin researchers conceded the plausibility of the main objections to twin method theory raised in Jackson's 1960 critique but continued to hold on to the method. But they were wrong, because it is theoretically impossible to have agreed with Jackson and also to have recognized the validity of the twin method.

Ironically, the validity of the schizophrenia twin studies and of the twin method itself was bolstered by the findings of the schizophrenia adoption studies. The widespread acceptance of these studies (particularly those carried out in Denmark) provided the twin method with a new lease on life, which has led to the current proliferation of twin studies and to the acceptance of psychiatric genetic and behavior genetic methods. This point was made explicit by Gottesman and Shields:

The difference in identical vs. fraternal twin concordance rates is not due to aspects of the within-family environment that are more similar for MZ than DZ twins, although there are many such aspects. Studies of MZ twins reared apart as well as adoption and fostering studies show a markedly raised incidence of schizophrenia among relatives even when they were brought up in a different home by nonrelatives. (1972, p. 318)

Thus, 12 years after the appearance of Jackson's critique, Gottesman and Shields (1972) cited the results of adoption studies as a way of arguing against the existence of environmental confounds in the twin method. In fact, there are serious problems with the schizophrenia adoption studies. In addition to methodological error and questionable diagnostic criteria, there is evidence that selective placement occurred in these studies on the basis of the psychiatric and socioeconomic status of experimental adoptees' biological families (see Cassou, Schiff, & Stewart, 1980; Joseph, 1999a, 1999b, in press-a; Lewontin, Rose, & Kamin, 1984). Thus, the likelihood that these children experienced inferior rearing environments compared with controls suggests that adoption studies are also vulnerable to environmental confounds.

Using today's behavior genetic terminology, Jackson essentially argued that the theoretical basis of the twin method—the MZ/DZ *equal environment assumption*—is false. In spite of attempts by twin researchers to provide theoretical and empirical justification for this assumption (e.g., Kendler, 1983), the equal environment assumption is as implausible today as it was when Jackson wrote about it (Joseph, 1998b). The conclusions drawn by researchers using the twin method, as with any other theoretical model, are based entirely on the assumptions underlying the method. If any one of these assumptions is violated or proven incorrect, the twin method would yield an entirely different set of conclusions. As noted elsewhere,

Any theoretical model is only as strong as its underlying assumptions. If the equal environment assumption is false, then the twin method becomes an instrument for the

measurement of the differing levels of association and environmental similarity between identical and fraternal twins. (Joseph, 1998b, p. 355)

In conclusion, Jackson's (1960) critique exposed the theoretical weaknesses of the classical twin method, which, he argued, is confounded by environmental factors. The use of the twin method for the detection of genetic influences is therefore of doubtful value. Jackson picked up a pen and wrote the obituary of the classical twin method, even if the world has been slow in realizing this fact.

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