

The Genetic Theory of Schizophrenia: A Critical Overview

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This article examines family, twin, and adoption studies supporting the widely accepted belief in the genetic basis of schizophrenia. Because results from family studies are consistent with a genetic or an environmental causation, emphasis is placed on twin and adoption studies. The validity of twin studies centers on the question of whether monozygotic/dizygotic concordance rate differences can be ascribed to genetic influences. This attribution rests on the assumption that identical and fraternal twins experience similar environments. There is good reason to doubt this assumption, and twin studies may only have measured the greater environmental similarity experienced by identical twins. Adoption studies also depend on a critical theoretical assumption: that factors relating to the adoption process (including the policies of adoption agencies) did not create conditions leading to a higher schizophrenia rate among experimental group adoptees. Evidence from the three regions where adoption studies took place suggests that potential adoptees with a family history of "mental illness" were placed into rearing environments inferior to those experienced by control adoptees. Twin and adoption studies have suffered from many other serious methodological problems. It is concluded that the evidence in favor of the genetic theory of schizophrenia is inconclusive, and that this theory should therefore be rejected until new evidence is presented in its favor. This analysis predicts that a gene for schizophrenia will not be found, because it does not exist.

Este artículo examina los estudios de familias, gemelos y adopción que apoyan la ampliamente aceptada creencia en la base genética de la esquizofrenia. Ya que los resultados de estudios de familias son consistentes con una causal genética o ambiental, el énfasis es puesto en los estudios de gemelos y adopción. La validez de estudios de gemelos se centra en la pregunta de si las diferencias en el índice de concordancia monozigótica/dizigótica pueden estar adscritas a influencias genéticas. Esta atribución se basa en la presunción que los gemelos idénticos y fraternales experimentan ambientes similares. Hay buena razón para dudar de esta presunción, y los estudios de

gemelos pueden haber medido solamente la semejanza ambiental más grande experimentada por gemelos idénticos. Los estudios de adopción también dependen de una presunción teórica crítica: que los factores relacionados al proceso adoptivo (incluyendo las políticas de las agencias de adopción), no crearon condiciones que condujeran hacia un nivel más alto de esquizofrenia entre los adoptados del grupo experimental. La evidencia de las tres regiones donde tuvieron lugar los estudios adoptivos sugiere que los adoptados potenciales con una historia familiar de "enfermedad mental" fueron puestos en ambientes de crianza inferiores a los experimentados por los adoptados del grupo de control. Los estudios de gemelos y adopción han sufrido de muchos otros problemas serios de metodología. Se concluye que la evidencia que favorece la teoría genética de la esquizofrenia es inconcluyente, y que, por eso, esta teoría debe ser rechazada hasta que se presente nueva evidencia a su favor. Este análisis predice que un gene para la esquizofrenia no será descubierto, porque no existe.

Cet article se penche sur les études familiales, de jumeaux et d'adoption qui sous-tendent la croyance en l'origine génétique de la schizophrénie. Les résultats des études familiales étant consistants avec une explication génétique ou environnementale, nous mettons ici l'accent sur les études de jumeaux et d'adoption. La validité des premières dépend du bien-fondé d'attribuer à une influence génétique les différences du taux de concordance entre jumeaux identiques et fraternels. L'attribution repose sur la présomption que ces deux types de jumeaux partagent des environnements similaires. Il existe cependant de bonnes raisons de douter de la justesse de cette présomption et les études de jumeaux n'ont peut-être mesuré que la plus grande similarité environnementale chez les jumeaux identiques. Quant aux études d'adoption, leur validité dépend aussi d'une présomption cruciale: que les facteurs liés aux processus d'adoption (ex., règlements en vigueur dans les agences d'adoption) n'ont pas contribué à augmenter le taux de schizophrénie chez les adoptés des groupes expérimentaux. Cependant, dans les trois régions où les études d'adoption ont été réalisées, tout indique que les adoptés potentiels avec une histoire familiale de "maladie mentale" ont été placés dans des foyers nettement inférieurs que ceux où ont été placés les adoptés des groupes témoins. Ces deux types d'études contiennent d'autres failles méthodologiques sérieuses. Il est ici conclu que l'évidence en faveur de la théorie génétique de la schizophrénie est inconcluante et qu'elle devrait donc être rejetée jusqu'à l'existence de nouvelles preuves en sa faveur. Cette analyse prédit qu'on ne découvrira jamais un gène de la schizophrénie, car il n'existe pas.

The purpose of this article is to evaluate the evidence in favor of the widely held belief that schizophrenia is acquired, at least in part, on the basis of genetic factors.¹ The question of whether schizophrenia carries a genetic predisposition is rarely debated anymore in the leading psychiatry and psychology journals. One could therefore conclude that the evidence in favor of the genetic perspective has been so overwhelming as to permanently resolve the issue, but as this article will demonstrate, this is not the case.

This is not the first time in the history of schizophrenia research that the question of genetic influences appears to have been “settled.” Before any twin, adoption, or even family study had been performed, a leading American psychiatrist and future schizophrenia twin researcher could write, based on the family histories of a few hospitalized patients, that “It would seem, then, that the fact of the hereditary transmission of the neuropathic constitution as a recessive trait, in accordance with the Mendelian theory, may be regarded as definitely established” (Rosanoff & Orr, 1911, p. 228). Six decades later, prominent schizophrenia researcher David Rosenthal would conclude from his adoption studies that the evidence is “so consistently and so strongly in favor of the genetic hypothesis that the issue must now be considered closed” (1970, pp. 131-132). More recently, others have claimed that “The substantial hereditary component in schizophrenia is surely one of the two or three best-established facts in psychiatry” (Bailey & Pillard, 1993, p. 241). In this article, it is asked whether such statements are supported by the evidence.

The most accepted causal framework for schizophrenia is called the “diathesis-stress theory” (Rosenthal, 1963). According to this theory, “what is inherited is a constitutional predisposition to schizophrenia” (p. 507). A person is viewed as inheriting a predisposition which will develop into schizophrenia in the presence of the necessary environmental triggers, which might include psychological factors, viruses, toxins, etc.

Today, schizophrenia researchers frequently claim that they have moved “beyond” twin and adoption studies, and that genetic linkage analysis and DNA studies should be the current focus of attention. However, the search for a “schizophrenia gene” is based on the implicit or explicit assumption that family, twin, and adoption studies have settled the question of the genetic nature of schizophrenia: the only problem left being the identification of the actual gene or genes (see, for example, Byerley & Coon, 1995; Jönsson et al., 1997). Unfortunately, attempts to find a genetic code underlying schizophrenia may be doomed because they presume the validity of evidence that in no way warrants uncritical acceptance. For example, the late 1980s saw the “discovery” of a gene for schizophrenia (Sherrington et al., 1988), but this claim could not be replicated (e.g., Kennedy et al., 1988).

SCHIZOPHRENIA FAMILY STUDIES

The genetic theory of schizophrenia found early support in the discovery of disturbed or psychotic people in the family histories (pedigrees) of diagnosed patients. Given the nonsystematic nature of such evidence, attempts were made to study the families of a large group of identified schizophrenics in order to determine whether the condition was found in greater numbers among their biological relatives than would be expected in the general population.

The first systematic schizophrenia family study (also known as a “consanguinity study”) was published in 1916, and more than two dozen have been performed since. Most of these studies were carried out by strong proponents of the genetic cause, most did not diagnose blindly, and many relied on hearsay or sketchy information in making diagnoses. Several modern family studies have

used control groups and blind diagnoses. Many of these studies have confirmed the findings of the older reports, but at least three (Abrams & Taylor, 1983; Coryell & Zimmerman, 1988; Pope, Jones, Cohen, & Lipinski, 1982) found no significant difference between the first-degree relatives of schizophrenics versus the expected population rate, or versus the rate among the first-degree relatives of controls. Although most consanguinity studies contained serious methodological flaws, it is likely that they do point to a familial clustering of schizophrenia. On the other hand, as Pam (1995) has noted, several studies resemble the now discredited accounts of familial "taint," such as the Kallikaks (Goddard, 1912) and the Jukes (Dugdale, 1887), whose "degeneracy" was traced through several generations and was assumed to have been genetic in origin, in spite of the likelihood that social, political, and psychological factors played a major role in the familial transmission of their status. In any case, it is remarkable that 89% of those diagnosed with schizophrenia have two parents who are not schizophrenic, and 63% have no first- or second-degree relatives with the diagnosis (Gottesman, 1991, pp. 102-103).

Most researchers carrying out consanguinity studies concluded that the familial clustering of schizophrenia proved or strongly suggested the existence of genetic factors. However, it is now acknowledged that familial clustering is consistent with both genetic *and environmental* explanations. At most, the role of genes is *implicated* by the finding that schizophrenia runs in families (Gottesman, 1991). As Rosenthal (1970) noted:

Although [family] studies are well worth undertaking for their own sake, the inference of a genetic basis must be held in abeyance until it can be shown that the association between incidence and consanguinity cannot be explained on some other basis. We might conceivably find a similar association with respect to some infectious diseases or with respect to a trait like poverty, where environmental factors may be of overriding importance. As a matter of fact, just such an association would be predicted by many clinical psychologists and psychiatrists who hold that the occurrence of functional behavior disorders results from peculiar or unusual behavior that takes place in certain families. (p. 37)

Indeed, the family is the primary means of transmitting values, ideas, and types of acceptable and unacceptable behavior from one generation to the next. According to Laing (1967), the family is "the usual instrument for what is called socialization, that is, getting each new recruit to the human race to behave and experience in substantially the same way as those who have already got here" (p. 43). Thus family studies provide inconclusive evidence of the role of genetic factors in the appearance of "psychopathology." As acknowledged by Gottesman, Rosenthal and others, family members share a common environment as well as common genes.

The recognition of the inconclusive nature of schizophrenia family studies led to the study of twins and adoptees as ostensibly better ways of testing for the possible role of genetic factors. These two methodologies, which the rest of this review discusses, have provided seemingly decisive evidence in support of the genetic theory of schizophrenia. An important question nevertheless remains: Do they stand up to critical reanalysis?

TABLE 1. Results of Published Schizophrenia Twin Studies

Study/Year	Country	Pairwise Concordance Rates					
		MZ Twins			Same-Sex DZ Twins		
		N	C	%	N	C	%
Luxenberger, (1928) [a]	Germany	17	10	59%	13	0	0
Rosanoff et al., (1934)	USA	41	25	61%	53	7	13%
Essen-Möller, (1941, 1970) [e]	Sweden	7	2	29%	24	2	8%
Kallmann, (1946)	USA	174	120	69%	296	34	11%
Slater, (1953)	UK	41	28	68%	61	11	18%
Inouye, (1961)	Japan	55	20	36%	17	1	6%
Tienari, (1963, 1975)	Finland	20	3	15%	42	3	7%
Gottesman & Shields, (1966a)	UK	24	10	42%	33	3	9%
Kringlen, (1967) [b]	Norway	45	12	27%	69	3	4%
NAS/NRC, (1970/1983) [c]	USA	164	30	18%	268	9	3%
Fischer, (1973) [d]	Denmark	25	9	36%	45	8	18%
Onstad et al., (1991)	Norway	24	8	33%	28	1	4%
Franzek & Beckmann, (1998) [f]	Germany	9	6	67%	12	2	17%
Cannon et al., (1998) [g]	Finland	—	—	—	—	—	—
Pooled Rates		646	283	44%	961	84	9%

C = Number concordant; N = Number of twin-pairs studied.

Concordance rates based on the authors' narrow definition of schizophrenia; Age correction factors not included.

Unless otherwise noted, when two dates are stated, the first indicates the year results were first published, the second indicates the final report, whose figures are reported in the table.

- [a] Based on figures provided by Gottesman & Shields (1966b, p. 14). Hospitalized co-twins only.
- [b] Based on a strict diagnosis of schizophrenia; hospitalized and registered cases.
- [c] National Academy of Sciences-National Research Council. Original report by Hoffer & Pollin, (1970); final report by Kendler & Robinette, (1983).
- [d] Final report of an expanded sample originally collected by Harvald & Hauge (1965).
- [e] MZ figures from Essen-Möller (1970). DZ figures were not reported in this paper. DZ concordance rate based on (1941) definite cases among co-twins, as reported in Gottesman & Shields (1966b, p. 28).
- [f] Concordance rates based on DSM-III-R schizophrenia in a twin having the same condition.
- [g] Cannon and associates (1998) reported probandwise concordance rates of 46% (MZ) and 9% (same-sex DZ). The pairwise equivalents of these figures are not listed in Table 1 because the number of pairs in each group was not given.

SCHIZOPHRENIA TWIN STUDIES

Overview

In order to assess the role that inherited factors play for a given trait, ability, or disease, the "classical twin method" (or "twin method") was invented. Inspired by the writings of Francis Galton (1875) and developed by Hermann Siemens (1924), the twin method has been promoted since the 1920s as a way

of determining whether a particular trait has a genetic component.² The method consists of comparing the concordance rates or correlations of reared-together identical twins (100% genetic similarity; also known as MZ, monozygotic, or one-egg twins) with the same measures of reared-together same-sex fraternal twins (averaging a 50% genetic similarity; also known as DZ, dizygotic, or two-egg twins). In psychiatric conditions such as schizophrenia, a significantly higher concordance rate among MZ twins when compared to DZ twins has been cited as evidence for the operation of genetic factors. Table 1 lists the 14 schizophrenia twin studies published through January, 1998. All pairs in these studies were reared together.

The pooled pairwise concordance rates across all studies in Table 1 are: MZ = 44%, DZ = 9%. Using more selective criteria, Torrey (1992, p. 163) calculated the pooled rates as: MZ = 28%, DZ = 6%. Gottesman (1991, p. 116) has arrived at similar figures: MZ = 31%, DZ = 9%.³

All of the studies were carried out by researchers who believed that schizophrenia carries a genetic component, and all researchers concluded that their results confirmed or were consistent with this belief. The group ranges from the fierce hereditarian Kallmann to advocates of an important role of psychodynamic factors, such as Tienari.

The results of these studies suggest that identical twins are significantly more concordant for schizophrenia than fraternal twins. Sample sizes vary dramatically (from 21 to 470 twin-pairs). Six of the studies (43%) were carried out in Scandinavian countries, and only one (Inouye) was conducted in a country where the majority of citizens are of non-European descent. Four of the first five studies (Essen-Möller, Kallmann, Luxenberger, Slater) were carried out by students of Ernst Rüdin's Institute of Psychiatric Research in Munich, Germany. Of the remaining studies, several were performed by people trained by members of this group (e.g., Fischer, Gottesman, Shields).

Fischer (1971, 1973), Gottesman and Bertelsen (1989), and Kringlen and Cramer (1989) have studied rates among the offspring of discordant monozygotic twins. Contrary to the claims of the proponents of the genetic theory, these studies are greatly flawed and no conclusions about the operation of genetic factors can be drawn from them. (See critiques of these studies in Joseph, 1998b, and Torrey, 1990.)

There have been no systematic studies of *separated* identical twins concordant for schizophrenia, but several individual case histories of ostensibly separated pairs have been reported. Farber (1981) performed an exhaustive review of these and other cases. She concluded that according to her "lenient criteria" (p. 165), 9 MZ pairs warranted consideration as legitimately separated twins. However, in all of these cases (6 pairs were considered concordant by Farber) the twins were aware of each other's existence and had periodic contact. The well-known report by Craike and Slater (1945) illustrates the arguable claim of "separation" common to most case histories. Farber considered this pair as "the best-separated set in the literature" (p. 156). Edith and Florence were British identical twins separated 9 months after birth. Florence was adopted by a maternal aunt, while Edith stayed with her father until the age of 8, when she was placed in a children's home. Although they did not meet again until age 24,

each was aware of the other's existence. Edith reported that while living with her father, "Florence was making trouble for her by writing to her father and telling him Edith had told her that he was a drunkard" (Craike & Slater, 1945, pp. 214-215). Edith also believed that Florence was watching her house and had been plotting against her. Their supposed delusional systems, which contributed to their schizophrenia diagnosis, centered on mutual distrust:

Each twin occupies for the other an overvalued position: *to each the other is supremely important* [italics added], although the circumstances of their lives touch at few points. Edith at first sight places Florence at the center of her persecutors; Florence, with her own inborn tendency to paranoia, reacts to this by coming in turn to regard Edith as her chief enemy. (Craike & Slater, 1945, p. 220)

Although Craike and Slater cited the twins' differing rearing environments as evidence in favor of the genetic theory of schizophrenia, it is clear that this "best separated set" had, in the words of Craike and Slater themselves, centered their "delusions around the other" (p. 221). It has been argued further that neither twin's symptoms warranted a diagnosis of schizophrenia (Pam, 1995; Ratner, 1982).

In closing, one must agree with the observations of many schizophrenia twin researchers that the case histories of separated identical twins concordant for schizophrenia represent little more than, as Gottesman (1991, p. 121) put it, "fascinating curiosities." He went on to add that "It's the kind of thing about which we should say, Lo and Behold—and then get on to other matters." (For a review of the problems with studies of separated twins, see Farber, 1981; Joseph, 1999; Kamin, 1974; Taylor, 1980.)

Criticism of Schizophrenia Twin Studies

Several critiques have been written of the twin method and its use in studying schizophrenia (Boyle, 1990; Cassou, Schiff, & Stewart, 1980; Jackson, 1960; Joseph, 1998a, 1998b; Lewontin, Rose, & Kamin, 1984; Pam, 1995). These critics have raised two major issues: (1) that methodological problems and bias have created inflated concordance rate figures, and (2) that comparisons of identical and fraternal twins are confounded by environmental factors.

It is clear that schizophrenia twin studies have suffered from serious methodological problems, such as the lack of an adequate and consistent definition of the dependent variable (schizophrenia), nonblinded diagnoses of schizophrenia, inadequate or biased methods of zygosity determination, the unnecessary use of age-correction factors, the use of nonrepresentative sample populations, and the lack of adequate descriptions of the methods used in some of the studies. However, these problems are not central to the validity of the schizophrenia twin studies, because there is little doubt that the MZ/DZ concordance rate difference for schizophrenia, as well as most other human behaviors, is real. The critical question centers on what is measured by this difference.

In 1960, Jackson wrote the first in-depth critique of the five schizophrenia twin studies then published. Jackson noted that, contrary to the predictions of

TABLE 2. DZ Same- and DZ Opposite-Sex Twin Pairwise Concordance Rates for Schizophrenia [a]

Study		Same-Sex	Opposite-Sex
Rosanoff et al., (1934) [b]	(DZ _{ss} = 5/53; DZ _{os} = 0/48)	9%	0%*
Kallmann, (1946)	(DZ _{ss} = 34/296; DZ _{os} = 13/221)	11%	6%**
Slater, (1953)	(DZ _{ss} = 11/61; DZ _{os} = 2/54)	18%	4%***
Inouye, (1961) [c]	(DZ _{ss} = 2/11; DZ _{os} = 0/6)	18%	0%
Harvald & Haugue, (1965) [d]	(DZ _{ss} = 4/33; DZ _{os} = 2/29)	12%	7%
Kringlen, (1967) [e]	(DZ _{ss} = 3/69; DZ _{os} = 3/64)	4%	5%
Totals:	DZ _{ss} = 59/523; DZ _{os} = 20/422	11.3%	4.7%****

* $p = .036$. ** $p = .019$. *** $p = .014$. **** $p = .0002$ (Fisher's Exact Test, one-tailed).

Weighted Z of all studies: 2.65, $p = .004$, one-tailed [f].

DZ_{ss} = Same-sex fraternal twins; DZ_{os} = Opposite-sex fraternal twins.

- [a] Cannon and associates (1998, p. 69) found the records of 163 opposite-sex DZ twin-pairs. Ten pairs (6.1%) were concordant for schizophrenia. The authors stated that these twins were ascertained in a different manner than the same-sex DZ pairs. Therefore they cannot be compared to the same-sex rate. Additionally, as noted in Table 1, the number of same-sex DZ pairs under study was not provided by Cannon and colleagues.
- [b] Based on twins sharing "similar affections" in Rosanoff and associates' Table 3 (1934, p. 269).
- [c] Based on figures reported in Gottesman & Shields (1966b, p. 50). Includes "schizophrenia and schizophrenia-like disorders," which were the only figures provided.
- [d] Preliminary report of the Danish sample. All other results from this sample are shown in Fischer's (1973) figures, which did not report DZs concordance rates.
- [e] Based on a strict definition of schizophrenia, hospitalized and registered cases.
- [f] This method (described by R. Rosenthal, 1991, pp. 90-98) determines a pooled significance level by dividing the sum of a study's p -derived weighted Z score ($N \times Z$) by the square-root of the summed squares of each study's N . Results falling in the nonexpected direction produce a negatively weighted Z score.

genetic theory about nonsex-linked conditions such as schizophrenia, female MZ pairs were more concordant than male MZ pairs; that female DZs were more concordant than male DZs; that DZ same-sex twins were more concordant than opposite-sex DZs; and that DZ twins were more concordant than ordinary siblings, despite sharing the same genetic relationship. Jackson (1960) put forward the idea that these differences, as well as the MZ/DZ concordance rate difference itself, could be explained by differing levels of environmental similarity and "ego-fusion":

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)

As an example of the likely environmental bias in schizophrenia twin studies, we will examine concordance rate differences between same-sex and

opposite-sex DZ twins. Although the twin method specifically compares MZ twin-pairs to *same-sex* DZ twins, several schizophrenia twin studies have collected data on concordance rates for opposite-sex DZ pairs as well. As observed by Jackson:

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)

The results shown in Table 2 (also discussed by Lewontin et al., 1984) list schizophrenia concordance rates for studies reporting on both types of DZ twins. Some studies listed concordance rates for the investigators' "broad" and "narrow" definitions of schizophrenia. Unless otherwise stated, concordance rates are based on the authors' narrow definition. In Table 2 we see that, contrary to genetic expectations, DZ same-sex twins are more than twice as concordant for schizophrenia as DZ opposite-sex twins. Additionally, the difference is statistically significant in three separate studies. One could reject the twin method as invalid on the basis of Table 2's numbers and an understanding of twin method assumptions (see below).

Proponents of the genetic theory of schizophrenia have not explained how concordance rate differences between these differing types of DZ twins can result from anything other than environmental factors. Typically, DZ same-sex/opposite-sex differences are simply acknowledged (e.g., Gottesman & Shields, 1966b, p. 76; Kallmann, 1946, p. 321; Plomin, DeFries, & McClearn, 1990, p. 339; Rosenthal, 1962, p. 406; Shields, 1968, p. 98), are ignored (e.g., Karlsson, 1966; Kendler, 1983, and other writings; Mittler, 1971), or are denied (e.g., Gottesman & Shields, 1982, p. 114; Keefe & Harvey, 1994, pp. 82-83).

Sex-based concordance rate differences highlight a common objection to the twin method: that, like family studies, it is unable to disentangle possible genetic and environmental factors. Proponents of the twin method have defended their claims on the basis of the validity of the so-called "equal environment assumption," which holds that the environments (or trait-influencing environments) of MZ and DZ twins are roughly the same (Kendler, 1983; Plomin et al., 1990). This assumption has been evaluated in at least two critical reviews (Joseph, 1998a; Pam, Kemker, Ross, & Golden, 1996), whose authors concluded that the assumption (and therefore the twin method) is not tenable. In fact, most schizophrenia twin researchers have acknowledged that concordance rate differences are affected by environmental factors (for documentation, see Joseph, 1998a).

Several studies have shown that identical twins share a more common environment than fraternal twins. Wilson (1934) found that MZ pairs spent more time together than DZs, and Smith (1965) found that MZ twins were more likely than DZs to, among other things, study together, dress alike, have the same close friends, and attend social events together. In Kringlen's 1967 twin study

report, there is an important yet rarely cited table showing the results of a survey looking at the environmental similarity and "ego fusion" of twins. Based on a sample of 75 MZ and 42 same-sex DZ pairs, Kringlen (p. 115) found that 91% of identical pairs had experienced "identity confusion in childhood," which was true for only 10% of the fraternal pairs. MZs were more likely to have been "brought up as a unit" than DZs (72% vs. 19%), and were more often "inseparable as children to an extreme degree" (73% vs. 19%). The final question made a global evaluation of twin closeness. For MZs, 65% were evaluated as having an "extremely strong" level of closeness, which was true for only 19% of the DZ twin-pairs. As we recall, Jackson (1960, p. 67) noted that the psychodynamic thesis predicts that "according to the degree of likeness in siblings, we will find an increased concordance for schizophrenia, without concern for genetic similarity." The results from Kringlen's survey lend strong support to this theory.

To summarize, 14 studies have demonstrated that identical twins are more concordant for schizophrenia than fraternal; what has *not* been demonstrated is that this difference records anything other than the greater environmental similarity and emotional bond experienced by MZ twins compared to DZ twins. The finding of genetic factors using the twin method depends upon the validity of the equal environment assumption, and the evidence suggests that this assumption is false. Like family studies, the twin method is clearly unable to disentangle possible genetic and environmental influences.

SCHIZOPHRENIA ADOPTION STUDIES

Overview

Dissatisfaction with the twin method among some genetically oriented researchers led to the study of adopted individuals as an ostensibly better way of separating genetic and environmental factors. Adoption studies are difficult to perform because of the scrupulously guarded records of both adoptees and their biological families. Unusual circumstances, such as the existence of national registers (Denmark) or the intervention of a U.S. senator (Heston, 1966) have usually been necessary to allow researchers access to needed records.

The results and conclusions of the schizophrenia adoption studies have played a crucial role in establishing the widespread acceptance of schizophrenia as a genetic disorder. As Neale and Oltmanns (1980) have written, if "any doubt remained concerning the importance of genetic factors in schizophrenia, it was abolished by the adoption studies" (p. 215). Schizophrenia adoption studies have been reported for over 30 years. There have been three principal research designs used in these studies, which are described below.

The Adoptees' Family Method. The Adoptees' Family Method (also known as the "Kety Strategy," or "Adoptee-as-Proband" method) begins with children given up for adoption who are later diagnosed with schizophrenia or a "schizophrenia spectrum disorder." (The Kety et al. 1968 spectrum included "chronic schizophrenia," "acute schizophrenia," "borderline or latent schizophrenia," "uncertain chronic schizophrenia," "uncertain acute schizophrenia," "uncertain

latent schizophrenia," "schizoid personality," and "inadequate personality.") A control group of nonschizophrenic adoptees is also established. It is then the task of the investigators to identify the biological and adoptive relatives in each group and to determine how many of these relatives are schizophrenic or have diagnoses within a defined schizophrenia spectrum. A significant difference between index and control biological relative spectrum diagnoses is considered evidence in favor of the genetic hypothesis.

The most important studies using this method have been performed in Denmark (Kety, Rosenthal, Wender, & Schulsinger, 1968; Kety, Rosenthal, Wender, Schulsinger, & Jacobsen, 1975). These reports were limited to the population of the greater Copenhagen area. The study was then extended to the rest of Denmark (Kety, Rosenthal, Wender, Schulsinger, & Jacobsen, 1978; Kety et al., 1994).

The 1968 study looked at the biological and adoptive relatives of 34 adopted-away children who were diagnosed with chronic schizophrenia (16), latent schizophrenia (11), and acute schizophrenia (7), and compared them with the relatives of 33 matched controls. All diagnoses were based on a blind evaluation of the participants' institutional records. The 1975 report utilized the same group of index and control adoptees (plus one additional control), but many relatives had now been interviewed and this information was supplied to the raters as part of the diagnostic process.⁴ The 1994 final report on the Provincial sample was also based on interviews, and the spectrum definition was narrowed to chronic schizophrenia and latent schizophrenia. All Adoptees' Family studies reported that, on the basis of a comparison of schizophrenia spectrum diagnoses among index versus control biological relatives (first- and second-degree), the significantly higher index rate demonstrated that genetic factors play an important role in schizophrenia. (For an in-depth critical analysis of these studies, see Joseph, 1998b; Lidz & Blatt, 1983.)

The Adoptees Method. Although the Kety strategy has been the most cited and discussed method, the Adoptees method (also known as the "Rosenthal Strategy," or "Parent-as-Proband" method) has been the most widely used. This method determines the rate of schizophrenia (or schizophrenia spectrum disorders) among the adopted-away children of schizophrenic parents (usually mothers). These adoptees are then compared to a control group of the adopted-away children of nonschizophrenic parents.

The first published schizophrenia adoption study (Heston, 1966) utilized the Adoptees method. Heston compared the offspring of schizophrenic mothers living in Oregon to the offspring of controls, and found a statistically significant difference between these two groups. The first paper reporting the results of this method in the Danish sample was published by Rosenthal and colleagues (1968). The follow-up to this report (Rosenthal, Wender, Kety, Welner, & Schulsinger, 1971) reported a statistically significant difference between the index and control group rates of spectrum disorders. The numerous problems with Rosenthal's study have been discussed in several critiques (e.g., Boyle, 1990; Joseph, 1998b; Lewontin et al., 1984; Lidz, Blatt, & Cook, 1981).

A third locus of Adoptees method investigation has been Finland, where the final report of a two-decade plus longitudinal study is nearing publication. The

research team is headed by P. Tienari, who holds the unique distinction of having performed both a schizophrenia twin and adoption study. The most recent update of the study's results was published in 1994 (Tienari et al., 1994). Tienari and colleagues are distinguished from Heston and the Danish/American group by virtue of their emphasis on studying family interaction effects as well as genetics. While presenting evidence claiming to support the genetic hypothesis, Tienari has noted that levels of adoptive family disturbance also predict which of his participants will become schizophrenic. According to Tienari and associates (Tienari, Sorri, et al., 1987, p. 482), "All adoptees who had been diagnosed either as schizophrenic or paranoid had been reared in seriously disturbed adoptive families." Like the Danish/American team, but unlike Heston, Tienari and associates (1997, p. 43) have created a "broad spectrum of nonschizophrenic psychotic illnesses" including nonpsychotic diagnoses such as schizo-typal personality disorder. (See Joseph, in press for a detailed critique of the Finnish adoption study.)

The Crossfostering Method. The Crossfostering method (also known as the "Wender Strategy") looks at the adopted-away children of nonschizophrenic biological parents who are raised by adoptive parents who become schizophrenic. The most important study utilizing this method was performed by Wender, Rosenthal, Kety, Schulsinger, and Welner (1974). Wender and colleagues compared their "crossfostered" group with the adopted-away children of normal biological parents reared by normal adoptive parents, and with a group of the adopted-away offspring of schizophrenic biological parents reared by normal adoptive parents. The Wender and associates 1974 paper is the weakest of the Danish/American studies, and will not be reviewed here. The reader is referred to the critiques of Boyle (1990), Joseph (1998b), Lewontin and colleagues (1984), and Lidz (1976).

A Brief Critique of the Schizophrenia Adoption Studies

All schizophrenia adoption studies have suffered from one or more of the following problems:

(1) *They have failed to seriously consider evidence of selective placement in their samples.* (See the discussion below.)

(2) *They have expanded the definition of schizophrenia to include a "schizophrenia spectrum" of disorders.* A careful analysis of the spectrum concept reveals that it is untenable on theoretical, empirical, and historical grounds. E. Bleuler, the inventor of the schizophrenia concept,⁵ believed that it was impossible to distinguish "milder cases of schizophrenia" from the merely "whimsical." "It is for this reason," continued Bleuler, "that the diagnostic threshold of schizophrenia is higher than that of any other disease" (E. Bleuler, 1911/1950, p. 294). There is reason to believe that Kety and colleagues created the spectrum concept due to the lack of chronic schizophrenia cases among those under study, and even by the Danish/American team's own criteria for

inclusion, no category other than chronic schizophrenia deserved to be counted as schizophrenia. In all Danish/American studies, the difference in chronic schizophrenia diagnoses between index and control first-degree biological relatives is not statistically significant. In fact, Kety and colleagues found only *one* index first-degree chronic schizophrenic biological relative in their 1975 interview-based study, and *zero* in the 1968 record-based report. (For a detailed discussion of these points, see Joseph, 1998b.)

(3) *They have failed to acknowledge that the rate of schizophrenia among index biological relatives must be significantly higher than the expected rate in the general population* (Boyle, 1990). Rosenthal (1974) has written that in order to “demonstrate that genes have anything to do with schizophrenia,” an investigator must show that “The frequency of schizophrenia [is] greater in the families of schizophrenics than in the families of nonschizophrenic controls or in the population at large” (p. 589). Rosenthal should have written “and” instead of “or,” because a greater index schizophrenia rate versus controls does not absolve the investigator of the responsibility of showing that this rate is also significantly greater than the expected general population rate. Boyle (1990) has made this point clear:

If the index biological relatives had a higher than expected prevalence of schizophrenia diagnoses *or* the control relatives were indistinguishable from the general population or the index relatives resembled the general population and the control relatives were exceptionally free from diagnoses, then significant differences, *but carrying very different interpretations* [italics added], could appear. (p. 141)

Boyle concluded that “a simple comparison of two groups of biological relatives does not indicate how similar each is to the general population” (p. 144).

(4) *They have failed to provide an adequate definition of schizophrenia or schizophrenia spectrum disorders.* Heston (who was not blind to the status of his adoptees) diagnosed schizophrenia on the basis of “generally accepted standards” (Heston, 1966, p. 82), while adding that the diagnosis “was used conservatively” (Heston & Denney, 1968, p. 369). The Danish/American diagnoses were made through the use of the “global diagnostic method,” which Kety and associates (1994, p. 445) could still not define 30 years after beginning their study. Tienari’s 1994 report was the first adoption study to use “operationalized” diagnostic criteria (DSM-III-R).

(5) *First- and second-degree relatives were counted equally in statistical calculations comparing index and control biological relatives.* Kety and associates (1975, p. 156) concluded that they had discovered “compelling evidence” for genetic factors by comparing the spectrum diagnosis rates of index and control biological paternal half-siblings. As discussed by Lidz and Blatt (1983), and demonstrated in a table published by Kety, Rosenthal, Wender, and Schulsinger (1976, p. 418), the difference is not statistically significant when the complete Danish/American spectrum (as defined by Kety et al., 1975, p. 154) is utilized. Several critics have questioned the Danish/American team’s strategy of counting half-siblings with the same weighting as first-degree relatives (e.g.,

Benjamin, 1976; Gottesman & Shields, 1976; Kringlen, 1976; Lidz & Blatt, 1983).

(6) *They have failed to provide an adequate number of case histories in their publications.* The Danish/American papers provided no case histories of any of their adoptees or relatives. Heston provided two brief descriptions, and Tienari and colleagues only a tiny handful. In contrast, several twin studies provided detailed case histories of their participants: in Kringlen's case, a 277-page case history companion volume. Written case histories afford reviewers the opportunity to know something of the conditions that adoptees and their relatives were raised under, and the symptoms they manifested.

Questions Concerning the Design of the Kety and Associates' Adoptees' Family Studies

Beginning with the 1968 study (first made public at the Dorado Beach schizophrenia conference in June/July, 1967), all Adoptees' Family reports have based their conclusions on the significant spectrum diagnosis difference between index and control biological relatives. However, questions have been raised about whether this comparison reflected the original research design of the Danish/American team. The design of the study was called into question by Lidz and Blatt (1983), who made the unsupported claim that the study's original intent had been to compare schizophrenia spectrum rates of index biological vs. *index adoptive* families. This claim was denied by Kety (1983). However, in a paper delivered in March, 1967, Rosenthal wrote that:

In Denmark, with the collaboration of Dr. Fini Schulsinger and others, we begin with adoptees who are now schizophrenic. *We compare the incidence of schizophrenic disorders in their biological and adoptive families* [italics added]. The same procedure is carried out for a matched group of normal adoptees, who serve as controls. (1967, p. 25)

Rosenthal is therefore on record as stating, in March of 1967, that the design of the study had been to compare the difference between index biological and index adoptive relatives *versus* the difference between control biological and control adoptive relatives—but it was not until April of 1967 that all of the data had been collected and diagnoses were made (Kety et al., 1968, p. 346). When comparisons are made using the method described by Rosenthal, it turns out that the difference is not statistically significant in either group. The Kety and colleagues record-based report (1968, p. 354) lists 13 spectrum diagnoses out of 150 *index biological relatives* (8.7%), and 2 such diagnoses out 74 *index adoptive relatives* (2.7%). A statistical comparison between these two groups shows that the difference is not significant ($p = .076$, Fisher's Exact Test, one-tailed). Therefore, had the Danish/American team analyzed their data using the approach described by Rosenthal—and there exists no other pre-1968 published Danish/American description of their method—they would have had to conclude that there were no significant differences between the groups, and that their study had found no evidence in support of the genetic theory of schizophrenia. Interestingly, Rosenthal's 1967 paper was not cited by Rosenthal or Kety in any of their subsequent publications on the genetics of schizophrenia.

Evidence of the Selective Placement of Adoptees

The idea of studying adopted-away children as a way of disentangling genetic and environmental factors is not as clear-cut as it may appear, for we must keep in mind that the population under study consists of children who have been given away by the people who had cared for them since birth. From the standpoint of genetically oriented researchers who are insensitive to the impact of parental abandonment and the psychological pain this act likely produces, the rupture of the parent/child relationship is of little importance. For those who believe that early childhood experiences are important, however, the adoption process may introduce special psychological circumstances.

In their critical analysis of the schizophrenia adoption studies, the French team of Cassou, Schiff, and Stewart (1980) repeatedly referred to these reports as "studies of abandoned children" ("Les Études d'Enfants Abandonnés"). As Pam (1995) has noted, this phrase indicates "the irony of using throwaway kids as proof that schizophrenia is genetically transmitted" (p. 31). Cassou and associates have posted a reminder that the decisive "evidence" in favor of the genetic theory of schizophrenia is based on the families of 150 or so abandoned Danish children.

Like the twin method, adoption studies are based on a critical theoretical assumption: that factors relating to the adoption process (including the policies of adoption agencies) did not lead to the placement of experimental (index) adoptees into environments contributing to a higher rate of the condition or trait in question. The placement of adoptees is assumed to have been random, meaning that children were not selectively placed into homes correlated with the status of their biological family. Lewontin, Rose, and Kamin (1984) have written that selective placement in adoption is:

[A] universal phenomenon in the real world in which adoptions in fact occur, and a phenomenon that undermines the theoretical separation of genetic and environmental variables claimed for adoption studies. The children placed into homes by adoption agencies are never placed randomly. For example, it is well known that biological children of college-educated mothers, when put up for adoption, are placed selectively into the homes of adoptive parents with higher socioeconomic and educational status. The biological children of mothers who are grade-school dropouts are usually placed into much lower-status adoptive homes. (p. 223)

Schizophrenia adoption studies have been carried out in three countries (Denmark, Finland, and the United States [Oregon]), and there is reason to believe that the children of families with a history of "mental illness" were not placed into the same types of homes as control adoptees, who typically lacked such a history.

In Denmark, two separate investigations (Hutchings & Mednick, 1975; Teasdale, 1979) found that the socioeconomic status of an adoptee's biological family was a factor influencing the matching process. Kety and colleagues (1994) have attempted to downplay the importance of this finding:

Since the etiological role of environmental variables remains obscure at present, it is not likely that a social agency, even if it set about doing so deliberately, could find sufficient of the unknown variables in the

prospective adoptive parents to materially affect the risk of [schizophrenic] illness in the adoptee. (p. 452)

Kety is asserting that simply because an agency does not know what kinds of environments lead to greater schizophrenia rates, it could not be placing certain children into more schizophrenia-producing environments. But is this really the case?

As an example of the potentially confounding influence of selective placement, there is pellagra, a disease characterized by digestive, skin, and nervous disturbances, followed by mental deterioration. In the early part of the 20th century, the disease was thought to have a strong inherited component, based on its tendency to cluster in certain families. It was later shown that pellagra is caused by the deficiency of a vitamin (Niacin) found in certain fruits and grains. It had occurred mainly in poor families, whose members did not eat enough of the foods supplying this needed vitamin. According to Kety's logic, an early 20th century adoption agency, unaware of the true causes of pellagra, could not have systematically placed certain classes of adoptees into more "pellagragenic" environments. However, if an agency had placed adoptees into homes corresponding to the socioeconomic status of the adoptee's biological family, then adoptees born into poor families would have been placed into poorer adoptive homes, where they would have been more likely to develop pellagra. All of this would have occurred without the adoption agency having any idea what the "unknown variables" of pellagra were. And Kety and associates (1994, p. 452) have acknowledged that schizophrenia, like pellagra, is correlated with lower socioeconomic status.

Denmark, in fact, has a long and ugly history of governmental and social support for eugenic practices⁶ and became the first European nation to pass national legislation for the purpose of promoting eugenic sterilization, predating the infamous Nazi sterilization law by four years. The 1929 legislation legalized sterilization and castration in cases of retardation or "mental illness." Although the word "eugenic" did not appear in the law, it allowed sterilization "where suppression of reproduction must be regarded of being of great importance to society" (Quoted in Hansen, 1996, p. 38). The law passed easily in the Danish Parliament and according to Hansen, "The Danish version of eugenics seemed to command agreement among all political parties" (p. 39). In 1935, a new law was passed permitting the compulsory sterilization of "mentally abnormal" people under certain circumstances (Hansen, 1996, p. 41). There were nearly 6,000 cases of sterilization for eugenic purposes performed in Denmark between 1929 and 1950. The castration and sterilization law was not revised until 1967, and legalized compulsory sterilization—but not necessarily the attitude supporting its use—was finally abolished.

Adoptees in the Danish/American studies were placed between 1924 and 1947 (Kety et al., 1968), meaning that the vast majority were given away at a time when the child of a "mentally ill" person was perceived as a carrier of "tainted" blood, that is, as a person who "did not deserve to be born." Kety and colleagues (1994, p. 453) have claimed that this aspect of the Danish adoption system did not play a role in the Adoptees' Family studies because "in practically every case" their index adoptees were born to *parents* with no record of

“mental illness” at the time of adoption. However, according to an annual report of one of the country’s largest adoption agencies, the records of *other family members* were checked as well:

Before a child is cleared for adoption, it is investigated with respect to health, and an attempt is made to obtain detailed information on the child’s family background and to form an impression of its developmental potential. Not only for the adoptive parents, but also for the child itself, these investigations are of great importance for its correct placement. Information is obtained on the child’s mother and father; *on whether or not there is serious physical or mental illness in the family background* [italics added]; criminal records are obtained for the biological parents; and in many cases school reports are obtained. By means of personal interview with the mother an impression of her is formed. Where information is uncovered on convicted criminality or on *mental retardation, mental illness, etc. in the family background* [italics added], the case is referred to the Institute of Human Genetics of Copenhagen University, with whom there exists a valuable cooperation for advice on the advisability of adoption. (Mother’s Aid Organization for Copenhagen, Copenhagen County and Frederiksborg County. Annual Report for 1946-47; Quoted in Mednick & Hutchings, 1977, p. 163)

As shown in this agency’s report, the fact that an adoptee’s biological parents had no record of “mental illness” at the time of adoption does not diminish the likelihood that placements were influenced by the prevalence of mental illness *among other family members*. As a demonstration of the likely effect such policies had on the types of homes adoptees were placed into, Lewontin and associates (1984) discovered that in 8 of the 33 index *adoptive* families, a parent had been admitted to a mental hospital, which was true for none of the control adoptive families. Selective placement was also a major factor confounding the results of Rosenthal’s Adoptees study, because *from either a genetic or environmental perspective*, the biological family of a schizophrenic or *future schizophrenic* would be expected to contain more individuals diagnosed with psychiatric disorders than a control biological family.

Eugenic sterilization laws were also on the books during most of the period when Tienari’s Finnish adoptees were being placed (Hietala, 1996; Joseph, in press). Like Denmark, Finland has a long history of eugenics-inspired legislation aimed at curbing the reproduction of people labeled mentally retarded and “mentally ill.”⁷ Eugenic ideas took root in Finland during the 1920s, and a government commission was created in 1926 to look into the desirability of promoting the sterilization of the “mentally ill” and the “mentally retarded,” although at that stage, few were calling for mandatory sterilization. By 1935, the Finnish Parliament had passed the Sterilization Act, which allowed the *compulsory* sterilization of “idiots,” “imbeciles,” and the “insane,” which included persons with diagnoses of schizophrenia and manic depression. The year 1950 saw the passage of the Castration Act, which permitted the compulsory castration of criminals, the mentally retarded, and the permanently “mentally ill.” It was not until the Abortion Act of 1970 that compulsory sterilization was legally abolished in Finland.

The adoptees in Tienari’s study were born between 1927 and 1979 (Tienari, Sorri, et al., 1987), and most were therefore placed during a period when

eugenic ideas were widespread in Finland and sterilization for eugenic purposes was permitted by law. Up to 33% of Tienari's index adoptees were born at a time when their mother's schizophrenia diagnosis was known (Tienari, Lahti, et al., 1987, p. 44). At an earlier point in the study, Tienari recognized the confounding effect that this knowledge could have on the adoption process, writing that "neither the child nor his adoptive parents should have had any contact with the child's biological mother, nor should they even have been aware of her psychosis" (Tienari, 1975, pp. 34-35).

Looking at Heston's 1966 investigation, the evidence of selective placement is even more apparent. All of Heston's index adoptees were born between 1915 and 1945 to actively schizophrenic mothers who were living in Oregon state mental hospitals. There were five cases of chronic schizophrenia among his 47 index adoptees, versus zero among 50 controls ($p = .024$). However, like Denmark and Finland, index adoptees were likely considered to be unwanted "taint-carriers." In 1917, a bill was passed in Oregon creating the State Board of Eugenics, whose duty was to authorize the compulsory sterilization of "all feebleminded, insane, epileptic[s] . . . who are persons potential to producing offspring who, because of inheritance or antisocial traits, would probably become a social menace" (Olson, 1920, p. 1487). Another Oregon law, passed in 1919, stipulated that the mere fact that a person had been admitted to a mental hospital constituted "prima facie evidence that procreation by any such person would produce children with an inherited tendency to feeblemindedness, insanity, epilepsy, criminality or degeneracy" (Olson, 1920, p. 3176). These laws were on the books until well after the last of Heston's adoptees were born. Consistent with the operation of selective placement of index adoptees into inferior rearing environments, Heston found a significantly greater rate of "psychosocial disability" (e.g., mental deficiency, sociopathic and antisocial behavior) among his index adoptees. For Heston, this finding suggested a genetic link between schizophrenia and psychosocial disability (Heston & Denny, 1968, p. 374).

If all schizophrenia adoption studies are considered in the context of the social and political environments from which they obtained their participants, the following can be concluded: *The great majority of adoptees under investigation by the schizophrenia adoption studies were given up for adoption at a time when the compulsory sterilization of "schizophrenics" for eugenic purposes was permitted by law in the country or state in which their adoptions took place (Denmark, Finland, Oregon).* Leaving aside all other problems, the evidence suggesting that the selective placement of adoptees occurred in these studies is reason enough to disregard their findings until evidence can be produced that such placements did not occur.

CONCLUSIONS

In summary, it is apparent that in addition to family studies, the classical twin method is unable to satisfactorily demonstrate that it can separate possible genetic and environmental influences on a particular condition or trait. It is therefore concluded that *there is no reason to accept that the twin method*

measures anything other than the environmental differences distinguishing identical and fraternal twins. The question does not center on the existence of MZ/DZ concordance rate differences, but instead on what is and is not measured by these differences.

The evidence suggests that the study of abandoned (adopted) children is also an inherently flawed method, at least in societies that match adoptees and adoptive parents on the basis of the socioeconomic and psychiatric status of the adoptee's biological family. It is abundantly clear that the methodological and theoretical flaws of the schizophrenia adoption studies render them suspect before any recalculation of their results is attempted.

Like Cassou and colleagues (1980, p. 197), it is concluded here that the total weight of evidence from family, twin, and adoption studies provides little or no evidence in favor of the genetic theory of schizophrenia. Remarkably, the only plausible evidence in favor of this theory is identical to that which existed before the first twin or adoption study had been undertaken: the observation that schizophrenia runs in families. The failure of schizophrenia twin and adoption studies to uphold the genetic hypothesis leads back to the question of whether familial clustering is due to common genes or common environment. Because this question remains unanswered, there is no proof that schizophrenia carries an inherited predisposition.

As known, scientists all over the world are searching for the genes believed to be involved in the development of schizophrenia. *Based on the weight of the evidence, it is predicted here that a gene for schizophrenia will not be found, because it does not exist.* Molecular biologists would do well to carefully reexamine the body of evidence upon which they have based their research. Future behavioral science investigators must focus attention on the environmental causes of schizophrenia, which likely constitute the entire explanation of the problem. The purpose here has been to challenge the consensus of opinion in favor of the genetic theory of schizophrenia (and by implication, other psychiatric diagnoses). If this review is able to play a role in reopening the debate, it will have served its purpose well.

NOTES

¹This paper does not address the validity of the schizophrenia concept, although the usefulness of this label, which Szasz (1976, p. xiv) considered "a concept wonderfully vague in its content and terrifyingly awesome in its implications," is certainly open to debate.

²On a historical note, Galton is known as the founder of the eugenics movement, which seeks to curb the reproduction of the carriers of allegedly "bad genes." Siemens's history is not as well-known, even though he is usually recognized as the discoverer of the twin method on the basis of his 1924 book, *Twin Pathology*. Like Rüdin, the founder of psychiatric genetics, Siemens was a leading figure in the German "Racial Hygiene" movement in the early to middle part of the 20th century, and was a supporter of the Nazi regime. In a forward to the 1937 (8th) edition of his book *Foundations of Genetics, Racial Hygiene, and Population Policy*, Siemens wrote: "since the National Socialist seizure of power [1933] the political goals that we, the race-hygienists, are in favor of, have now become a part—and not the least important one—of the German government

program. 'Race hygiene as a utopian dream' became 'Race hygiene as political program'. . . . Our future will be governed by race hygiene—or it will not exist at all" (Forward to Siemens, 1937). Later in the 8th edition, Siemens discussed how Galton's ideas were being put into practice in Germany:

Galton already saw the possibility of integrating race-hygienic ideals—just like a new religion—into the national conscious. The national [völkische] state, however, is now called on to be really serious about it. According to its *Führer*, it is the obligation of the national state 'to declare children as a people's most precious commodity' so that 'it will one day be considered reprehensible to withhold healthy children from the nation' [Hitler]. (Siemens, 1937, p. 180)

Siemens lived in the Netherlands during the Nazi period, so the views expressed in his writings cannot be attributed to the pressures of living under the regime. Although postwar editions of his books removed statements in support of Hitler's policies, according to Proctor (1988), the 1952 edition of Siemens's book "continued to advocate the forcible sterilization of inferior stocks" (p. 306).

³Gottesman is an advocate of the so-called probandwise method of concordance rate calculation. His pooled estimate was given as probandwise rates of MZ = 48%, DZ = 17%. The rates quoted in the present review are the pairwise equivalents of these figures.

⁴The Kety and associates 1975 report has been typically referred to as the interview-based study, but this is somewhat of a misnomer. In fact, only 64% of the 347 identified biological relatives and 48% of the identified adoptive relatives were actually interviewed (Kety et al., 1975, p. 151). The Danish/American team has frequently stated that 90% of all *available* relatives agreed to an interview, while they downplayed the fact that only 72% were alive and accessible. As it turns out, many of the 1968 biological relatives had died (20% index and 13% control). An additional 10.5% had emigrated outside of Scandinavia or had disappeared. Similarly, only 63% of the biological relatives in the Kety and colleagues (1994) Provincial study were interviewed (p. 445). Although not discussed in any Danish/American publication, several "pseudo-interviews" were prepared for adoptees and relatives. According to Lewontin and associates (1984):

[I]n several cases, when relatives were dead or unavailable, the psychiatrist "prepared a so-called pseudo interview from the existing hospital records." That is, the psychiatrist filled out the interview form in the way in which he guessed the relative would have answered. (p. 225)

In other words, the Danish members of the team *made up* interviews for several adoptees and relatives. According to Kendler and Gruenberg (1984), the authors of an independent reanalysis of the study,

Based on an extensive review of hospital records, detailed pseudointerviews were constructed for all of the index adoptees. These pseudointerviews contained more detailed information on the index adoptees than had been available to Kety and coworkers when they made their initial [1968] diagnoses. However, although they contained a detailed account of the psychiatric illness, the hospital records did not contain all the information normally present in sections of the real interviews dealing with such factors as personal history or living environment. This difference in information content as well as other differences in format *made it impossible to be "blind" to*

whether an adoptee interview was a real interview with a control adoptee or a pseudointerview with an index adoptee [italics added]. (p. 556)

Based on this revelation, it appears that Kety and colleagues' interview diagnoses were not as blind as they had implied. Kendler and Gruenberg have written that they could tell the difference between a real and a "pseudo" interview based on hospital records, and one could reasonably assume that Kety, Rosenthal, and Wender also noticed the difference. Because Kety and associates had known from the 1968 records that many more index than control biological relatives had been hospitalized, the recognition of a pseudointerview based on hospital records introduced a bias into the diagnostic procedure because this participant would have likely been an index relative.

⁵As an example of Kety and associates' reliance on Bleuler, here is Kety in 1985:

[W]e also took into account Bleuler's description of the symptoms of latent schizophrenia as he observed them in the relatives of overt schizophrenia patients. Bleuler's description of latent schizophrenia actually was the most useful guide since only those observations, like ours, had been made on individuals not hospitalized or seeking treatment. (Kety, 1985, p. 592)

⁶This discussion is based largely on the historical research of Hansen (1996).

⁷The discussion of eugenic ideas and laws in Finland is based in large part on the work of Hietala (1996).

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