Chapter 7

# Schizophrenia and heredity

## Why the emperor has no genes

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In 1990, psychologist Richard Marshall asked whether the genetic basis of schizophrenia is best understood as an axiom or a hypothesis. The position of mainstream psychiatry and psychology, as seen in countless books, articles, and textbook chapters, is that it is axiomatic. This position is based on the acceptance of the results of schizophrenia family, twin and adoption studies. Concurrently, the ongoing search for 'schizophrenia genes' is contingent upon the acceptance of these studies. The purpose of this review is to show that, contrary to prevailing opinions, the available evidence provides little support for a genetic basis or predisposition for schizophrenia. The fruitless search for genes (Bassett *et al.* 2001) is best understood by the failure to critically re-examine the literature upon which it is based, rather than the difficulty of finding schizophrenia genes.

### FAMILY STUDIES

Family studies locate persons affected with a particular trait or condition and determine whether their biological relatives are similarly affected more often than members of the general population or a control group. If a condition is found to cluster or 'run' in families, it is said to be familial. Many people view the terms 'familial' and 'genetic' as being synonymous. They are not. Although the familiality of schizophrenia was once seen as positive proof that schizophrenia is a genetic disorder, most investigators now realize that conditions or behaviours can run in families for reasons such as exposure to common rearing patterns, and other aspects of the physical and social environment. For this reason, psychiatric genetics has turned to twin and adoption studies

### TWIN STUDIES

The logic of the twin method seems straightforward: If reared-together monozygotic (identical) twins, who share 100% of the same genes, are

*Table 7.1* Results of schizophrenia twin studies published before mid-2001

| | | Pairwise concordance rates | | | | | |
|---|---|---|---|---|---|---|---|
| | | Monozygotic twins | | | Same-sex dizygotic twins | | |
| *Study* | *Country* | *N* | *C* | % | *N* | *C* | % |
| **Classical studies** | | | | | | | |
| Luxenburger (1928)[a] | Germany | 17 | 10 | 59 | 13 | 0 | 0 |
| Rosanoff *et al.* (1934) | USA | 41 | 25 | 61 | 53 | 7 | 13 |
| Essen-Möller (1941, 1970)[b] | 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 |
| **Contemporary studies** | | | | | | | |
| Tienari (1963, 1975) | Finland | 20 | 3 | 15 | 42 | 3 | 7 |
| Gottesman and Shields (1966b) | UK | 24 | 10 | 42 | 33 | 3 | 9 |
| Kringlen (1967)[c] | Norway | 45 | 12 | 27 | 69 | 3 | 4 |
| NAS-NRC (1970/1983)[d] | USA | 164 | 30 | 18 | 268 | 9 | 3 |
| Fischer (1973)[e] | Denmark | 25 | 9 | 36 | 45 | 8 | 18 |
| Koskenvuo *et al.* (1984)[f] | Finland | 73 | 8 | 11 | 225 | 4 | 2 |
| Onstad *et al.* (1991) | Norway | 24 | 8 | 33 | 28 | 1 | 4 |
| Franzek and Beckmann (1998)[g] | Germany | 9 | 6 | 67 | 12 | 2 | 17 |
| Cannon *et al.* (1998)[h] | Finland | — | — | — | — | — | — |
| **Pooled rates** | | 719 | 291 | 40.4 | 1186 | 88 | 7.4 |
| Classical studies | | 335 | 205 | 61.1 | 464 | 55 | 11.9 |
| Contemporary studies | | 384 | 86 | 22.4 | 722 | 33 | 4.6 |

*Note*: Concordance rates based on the authors' narrow or 'strict' 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 and the second indicates the final report, whose figures are reported here. *N* = number of twin pairs studied, *C* = number concordant.

[a] Based on figures found in Gottesman and Shields (1966a); hospitalized co-twins only.
[b] Identical twin figures from Essen-Möller (1970). Fraternal twin figures were not reported in this paper. Fraternal twin concordance rate based on 1941 definite cases among co-twins, as reported in Gottesman and Shields (1966a: 28).
[c] Based on a strict diagnosis of schizophrenia; hospitalized and registered cases.
[d] National Academy of Sciences/National Research Council. Original report by Hoffer and Pollin (1970); final report by Kendler and Robinette (1983).
[e] Final report of an expanded sample originally collected by Harvald and Haugue (1965).
[f] The study of Koskenvuo *et al.* (1984) is rarely mentioned in textbooks or reviews.
[g] Concordance rates based on DSM-III-R schizophrenia in a twin having the same condition.
[h] Cannon *et al.* (1998) reported probandwise concordance rates of 46% (identical) and 9% (same-sex fraternal). The pairwise equivalents of these figures are not listed here because the number of pairs in each group was not reported by Cannon *et al.*

significantly more concordant for schizophrenia than reared-together same-sex dizygotic (fraternal) twins, who share on average only 50% of the same genes, then the genetic position is confirmed. Table 7.1 lists all schizophrenia twin studies before mid-2001.

As shown in Table 7.1, the pooled pairwise concordance rates for schizophrenia are 40.4% monozygotic and 7.4% dizygotic. Schizophrenia twin studies are often divided into the 'classical' studies published before 1962 and the more methodologically sound 'contemporary' studies published after this date (Gottesman 1991; Neale and Oltmanns 1980). We can see that the older, more methodologically suspect classical studies, using non-blind diagnoses and potentially biased resident hospital samples (e.g. Kallmann 1946; Rosanoff *et al.* 1934; Slater 1953), reported higher rates than the more recent studies based on registers or consecutive hospital admissions. In these more recent studies, beginning with Tienari (1963, 1975), the pooled pairwise concordance rate falls to 22.4% monozygotic and 4.6% dizygotic. Identical twin concordance is 18% or less in three of the contemporary studies, as well as in two studies with large monozygotic samples. Nevertheless, twin researchers argue that the modern studies support the genetic position on the basis of a monozygotic concordance rate four to five times higher than the same-sex dizygotic rate (Torrey 1992; Walker *et al.* 1991).

## The equal environment assumption

There are several methodological problems with the schizophrenia twin studies. These include: (1) lack of an adequate and consistent definition of schizophrenia; (2) non-blinded diagnoses, often made by investigators strongly devoted to the genetic position; (3) diagnoses made on the basis of sketchy information; (4) inadequate or biased methods of zygosity determination (that is, whether twins are monozygotic or dizygotic); (5) unnecessary age-correction formulas; (6) non-representative sample populations; and (7) lack of adequate descriptions of methods.

Although these are important problems, there is little doubt that monozygotic twins are more concordant than dizygotic twins for schizophrenia and most psychological traits. This leads to a major problem. The twin method is based on a crucial theoretical assumption, which holds that the environments of monozygotic and dizygotic twins are about the same. However, this 'equal environment assumption' has little basis in the evidence. Monozygotic twins' more similar social and physical environments contribute to monozygotic–dizygotic concordance rate differences (Joseph 1998, 2003). Because it is widely understood that monozygotic twins are treated more similarly, encounter more similar environments, and experience greater 'identity confusion' (Jackson 1960) than dizygotic twins, there is no reason to accept that monozygotic–dizygotic comparisons measure anything more than the *environmental* differences distinguishing the two types of twins.

Rather than accepting this obvious conclusion, twin researchers subtly redefined the equal environment assumption by adding the following

provision: Although monozygotic twins were acknowledged to experience much more similar environments than dizygotic twins, critics must demonstrate that monozygotic and dizygotic twins' environments differ 'in respects which can be shown to be of etiological significance for schizophrenia' (Gottesman and Shields 1972: 25). This new definition, generally referred to as the 'trait-relevant equal environment assumption', has been promoted by many contemporary twin researchers. However, what these investigators fail to understand is that *the trait-relevant equal environment assumption has transformed the twin method into nothing more that a special type of family study*. This is because the comparison groups in both family studies and the twin method (in family studies, the general population or a control group; in the twin method, dizygotic twins) are acknowledged to experience different environments than the experimental groups (in family studies, the families of people diagnosed with schizophrenia; in the twin method, monozygotic twins). Why, then, do twin researchers retain the trait-relevant requirement for the twin method but *not* for family studies? Virtually every argument made by twin researchers in defence of drawing genetic inferences from monozygotic–dizygotic comparisons could also be made in defence of drawing genetic inferences from family studies. Yet, strangely, these investigators arbitrarily uphold the validity of the equal environment assumption and the twin method in the same breath as they admit that family studies are confounded by environmental factors.

Additional evidence against the equal environment assumption in the schizophrenia twin studies can be found elsewhere (see Jackson 1960; Joseph 1998, 2001b, 2003; Pam *et al.* 1996; Rose *et al.* 1984). The crucial point is that genetic inferences drawn from monozygotic–dizygotic comparisons are dependent upon an unsupported and counterintuitive theoretical assumption. Therefore, the twin method is confounded by environmental factors and cannot tell us anything about possible genetic influences on schizophrenia.

## Other twin studies

Two other types of twin studies should be mentioned. The first type (Fischer 1971, 1973; Gottesman and Bertelsen 1989; Kringlen and Cramer 1989) studied rates of schizophrenia among the offspring of *discordant* monozygotic twins. (The genetic position predicts that the rate of schizophrenia should be the same among the offspring of monozygotic twins diagnosed with schizophrenia, as among the offspring of their 'well' monozygotic co-twins.) However, these studies were seriously flawed, and no valid conclusions about the role of genetic factors can be drawn from them (Joseph 2003; Torrey 1990).

The second method consists of single-case reports of concordant monozygotic twins whom the researchers regard as having been reared apart (in

many cases, this is a very questionable claim; Joseph 2001c, 2002, 2003). Because the number of such pairs is small and because of the inherent bias in these types of reports, contemporary twin researchers do not place much value in them. As Gottesman (1982) concluded, 'After a quarter century of experience with twins reared together and twins reared apart, it is my conviction that twins reared apart are a wonderful source of hypothesis generation, but not a useful source for hypothesis testing' (p. 351).

## ADOPTION STUDIES

Adoption studies have played a crucial role in establishing schizophrenia as a genetic disorder. Moreover, the early studies performed in Oregon and Denmark helped pave the way for the acceptance of an important role for genetic factors in shaping human psychological and behavioural differences in general. For Gottesman and Shields (1976), the early adoption studies of schizophrenia were 'the straw that broke the environmentalist's back' (p. 364).

There have been six major schizophrenia adoption studies. In the first, Heston (1966) compared the rate of schizophrenia among 47 adopted-away offspring of women diagnosed with schizophrenia who were confined to Oregon state mental hospitals, with a control group of 50 adoptees of non-diagnosed mothers. In the second, Rosenthal and colleagues (1968, 1971) studied the adopted-away offspring of parents diagnosed with schizophrenia, 'schizophrenia spectrum disorders' or manic depression. In the third, and using a different design, Kety and colleagues (1968) began with the records of adoptees from the greater Copenhagen area, identified those diagnosed with a schizophrenia spectrum disorder, and recorded diagnoses among their adoptive and biological relatives. In a follow-up (Kety *et al.* 1975), the investigators interviewed and re-diagnosed many of the 1968 relatives. The study was then extended to the rest of Denmark and the final results were published in 1994 (Kety *et al.* 1994).

The fourth major schizophrenia adoption study was the Danish–American 'cross-fostering' study of Wender and colleagues (1974). They studied the adopted-away children of non-schizophrenic biological parents, who were raised by an adoptive parent eventually diagnosed with schizophrenia. According to the investigators, the purpose of the study was to 'explore the hypothesis that rearing by or with schizophrenic parents will produce schizophrenic psychopathology among persons who carry a normal genetic load' (Wender *et al.* 1974: 122). This 'crossfostered' group was compared with the adopted-away children of normal biological parents (who were reared by normal adoptive parents), and with a group of adopted-away offspring of schizophrenic biological parents reared by normal adoptive parents.

The final study was performed by Tienari and colleagues (1987, 2000) in Finland. In contrast to the earlier investigations, Tienari and colleagues studied adoptees' family environments as well their genetic background. The Finnish study is by far the most methodologically sound and comprehensive schizophrenia adoption study.

The following results are taken from a 2000 publication by Tienari and colleagues. Of the 164 index adoptees, whose biological mothers were diagnosed with DSM-III-R schizophrenia or paranoid psychosis, 11 (6.7%) received a DSM-III-R schizophrenia diagnosis, whereas there were 4 (2.0%) such diagnoses among the 197 control adoptees. Tienari and colleagues created a 'narrow spectrum' of supposedly related disorders, which included 'schizoaffective disorder', 'schizophreniform disorder' and 'schizotypal personality disorder'. They also made diagnoses for a 'broad spectrum', which included the above diagnoses plus 'paranoid personality disorder', 'schizoid personality disorder', 'delusional disorder', 'bipolar psychosis' and 'depressive psychosis'. The index 'narrow' and 'broad' spectrum rates were statistically significant versus the control group rates.

The investigators concluded, 'The genetic liability to "typical" DSM-III-R schizophrenia is decisively confirmed. Additionally, the liability also extends to a broad spectrum of other psychotic and non-psychotic disorders' (Tienari *et al.* 2000: 433). If we limit the comparison to mothers and offspring diagnosed with DSM-III-R schizophrenia, however, the study produces different results. According to unpublished results graciously provided by Tienari, DSM-III-R schizophrenia was diagnosed in 7 of 137 adoptees (5.1%) whose biological mothers were also diagnosed with DSM-III-R schizophrenia, compared with 3 of 192 (1.6%) control DSM-III-R schizophrenia diagnoses (P. Tienari, personal communication). Therefore, the index–control DSM-III-R schizophrenia difference is not statistically significant (7/137 compared with 3/192, $p = 0.065$, Fisher's exact test, one-tailed). In another paper emanating from this study, Wahlberg and associates (2000) compared the scores of a subsample of index and control adoptees on the Thought Disorder Index (TDI). The results showed no significant differences between index and control adoptee TDI scores, and that both groups' scores were about the same as those of normal individuals. On the basis of other comparisons, however, Wahlberg and colleagues concluded that genetic factors influence some components of thought disorder.

Tienari and associates concluded that both genes *and* adoptive family rearing environment are 'predictor variables' for schizophrenia. The investigators found that index adoptees who grew up in seriously disturbed adoptive families are diagnosed with schizophrenia more often than control adoptees reared in seriously disturbed families. Thus,

> the results were consistent with the hypothesis that healthy rearing families have possibly protected the vulnerable children, whereas in

> disturbed rearing families the vulnerable children have been more sensitive to dysfunctional rearing.
>
> (Tienari *et al.* 1994: 23)

The correlation between adoptive family disturbance and index adoptee schizophrenia cases was so great that, at least through 1987, Tienari could report that 'all adoptees who had been diagnosed either as schizophrenic or paranoid had been reared in seriously disturbed adoptive families' (Tienari *et al.* 1987: 482).

## Methodological problems

In all schizophrenia adoption studies, the investigators concluded that they found evidence to support important genetic influences on schizophrenia, while Tienari and colleagues added a finding that disturbed family environments also contributed to the condition. However, these studies have been the subject of several critical analyses questioning the investigators' methods and conclusions (Benjamin 1976; Boyle 1990; Breggin 1991; Cassou *et al.* 1980; Cohen and Cohen 1986; Gottesman and Shields 1976; Joseph 1999a, b, 2000a, 2001a, 2003; Rose *et al.* 1984; Lidz 1976; Lidz and Blatt 1983; Lidz *et al.* 1981; Pam 1995). These authors' criticisms of the schizophrenia adoption studies include the following:

- Most of these studies would not have found statistically significant differences without greatly expanding the definition of schizophrenia to include non-psychotic 'schizophrenia spectrum disorders'. The 1968 study of Kety *et al.* found *no* cases of chronic schizophrenia among the 65 identified first-degree biological relatives of adoptees diagnosed with a spectrum disorder. Rosenthal *et al.* (1971) found that only one of the 76 adopted-away biological offspring of parents diagnosed with a spectrum disorder had received a hospital diagnosis of schizophrenia.
- There was a failure to adequately define schizophrenia and schizophrenia spectrum disorders.
- In the 1971 study of Rosenthal *et al.*, manic depression was included in the schizophrenia spectrum in spite of the investigators' insistence elsewhere that this condition is genetically unrelated to schizophrenia (see Kety *et al.* 1976; Rosenthal 1971).
- In the interview studies of Kety *et al.*, there were inconsistencies in the way that dead or unavailable relatives were counted and diagnosed.
- There was a failure to provide case history information on adoptees or relatives and, apart from Tienari, to study important environmental variables.
- In the studies of Kety *et al.*, the 'procedure of counting up all the possible relatives of each index case and pooling them as if they were

independent samples . . . would allow some families to disproportionately affect the results' (Benjamin 1976: 1130). Thus, the investigators' decision to emphasize the spectrum rate among individual *relatives*, as opposed to individual *families*, violated the assumption of independent observations underlying their statistical comparisons.

- First- and second-degree relatives were counted with equal weighting in the studies of Kety *et al.*
- In the Denmark and Oregon studies, the genetic bias of the investigators influenced the way that relatives were counted, the way schizophrenia was defined, the types of comparisons made and the conclusions that were reached.
- Many late-separated adoptees were included in the samples.
- In the studies of Kety *et al.*, many of the 'interviews' never took place and were simply fabricated by the investigators (Kendler and Gruenberg 1984; Rose *et al.* 1984). In the raw data they were called 'pseudo-interviews' by Kety *et al.*, but no mention of them appeared in any of the Danish–American investigators' publications. Of the interviews that were conducted, a five-minute doorstep conversation was deemed sufficient to diagnose someone with schizophrenia (Paikin *et al.* 1974).
- Problems with Wender and colleagues' (1974) cross-fostering study include: (1) use of global mental health ratings in place of diagnosing schizophrenia; (2) *post-hoc* comparisons to support the genetic position; (3) failure to find statistically significant differences between important comparison groups; (4) failure to consider alternative explanations of results; and (5) the mean age of the cross-fostered adoptees at the time their adoptive parents were diagnosed with a spectrum disorder was 12 years (based on a subsample reported by Van Dyke *et al.* 1975). By the 1980s, Wender himself admitted that, in his 1974 study, 'the question of what would happen if children born of normal parents were placed in the homes of typical schizophrenics cannot be answered' (Wender and Klein 1981: 175).
- Failure to pay serious attention to the likelihood that the selective placement of adoptees biased the results of the studies.

Table 7.2 summarizes the presence or absence of important methodological problems in each study.

*Table 7.2* Important methodological problems of the schizophrenia adoption studies

| | Significant chronic schizophrenia Studied | Significant chronic schizophrenia Counted |
|---|---|---|

## Selective placement: the problem that won't go away

Like the twin method, adoption studies have their own crucial theoretical assumptions. The most crucial is the assumed absence of selective placement, meaning that both index and control adoptees had equal chances of being placed into the range of available adoptive homes. In the

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*Table 7.2* Important methodological problems of the schizophrenia adoption studies

| *Study* | *Country* | *Significant chronic schizophrenia first-degree bio relative rate vs controls?*[a] | *Significant chronic schizophrenia first-degree bio family rate vs controls?*[b] | *Used late separated adoptees?* | *Probable selective placement bias?* | *Blind diagnoses?* | *Adequate definition of schizophrenia?* | *Used a schizophrenia spectrum?* | *Studied adoptive family-rearing environments?* | *Adequate case history information provided?* | *Used fabricated interviews to make diagnoses?* | *Counted first- and second-degree relatives equally?* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Heston (1966) | USA (Oregon) | Yes | N/A | No | Yes | No[c] | No | No | No | No | No | N/A |
| Kety *et al.* (1968) | Denmark | No | No | N/A | Yes | Yes | No | Yes | No | No | N/A | Yes |
| Kety *et al.* (1975) | Denmark | No | No | N/A | Yes | Yes | No | Yes | No | No | Yes[e] | Yes |
| Kety *et al.* (1994) | Denmark | Yes | No | N/A | Yes | Yes | No | Yes | No | No | ? | Yes |
| Rosenthal *et al.* (1968, 1971) | Denmark | No | N/A | Yes | Yes | Yes | No | Yes | No | No | No | N/A |
| Wender *et al.* (1974) | Denmark | No | N/A | Yes | Yes | Yes | No | Yes | No | No | No | N/A |
| Tienari *et al.* (1987, 2000) | Finland | No | N/A | Yes | Yes | Yes | Yes[d] | Yes | Yes | No | No | N/A |

*a* Using the traditional one-tailed 0.05 level of statistical significance utilized by all schizophrenia adoption researchers. Based on a comparison between: (1) the first-degree biological relatives of chronic schizophrenia index adoptees *vs* the first-degree biological relatives of control adoptees (Kety); (2) the chronic schizophrenia rate among the adopted-away biological offspring of people diagnosed with chronic schizophrenia *vs* the biological offspring of controls (Heston, Rosenthal, Tienari); or (3) the chronic schizophrenia rate of crossfostered adoptees *vs* controls (Wender).

*b* Based on a comparison between the biological families of index adoptees diagnosed with chronic schizophrenia, with at least one first-degree biological relative diagnosed with chronic schizophrenia *vs* the biological families of controls with at least one first-degree biological relative diagnosed with chronic schizophrenia.

*c* Although two of the three raters made diagnoses while unaware of the adoptees' group status, the third rater, Heston, was not blind to their status.

*d* Although the validity of the DSM-III-R criteria (used by Tienari) is questionable, this is the only study to use clear and accepted diagnostic guidelines.

*e* For documentation of Kety and colleagues' use of fabricated 'pseudo-interviews', see Rose *et al.* (1984: 224) and Kendler and Gruenberg (1984: 556). It is not clear whether Kety *et al.* used pseudo-interviews in the 1994 study.

schizophrenia adoption studies, the likelihood that the adoptees' biological background influenced adoption placements is a major potentially invalidating factor.

The adoptees under study were placed in the early-to-middle part of the twentieth century in Denmark, the United States (Oregon) and Finland. However, all three regions had laws which permitted the compulsory eugenic sterilization of people diagnosed with schizophrenia and other 'mental disorders'.

### Denmark

In 1929, Denmark became the first European nation to pass a eugenics-inspired sterilization law, and a more comprehensive statute was passed in 1935 (Hansen 1996). These laws were in force until well after the last studied Danish adoptees were placed (placements were made between 1924 and 1947). An investigator with intimate knowledge of the Danish adoption process wrote, 'Every weekend (at least in the 1930s), Danish people who wished to adopt would visit the orphanages and pick children' (Mednick 1996: 134). There were many more available children than there were available adoptive parents (Mednick *et al.* 1987). The Danish adoption agencies clearly stated that a potential adoptee's genetic family background was checked to determine suitability (or desirability) for adoption (Mednick and Hutchings 1977). One can conclude that the most qualified potential adoptive parents, who were usually informed of 'deviance' in the adoptee's family background (Mednick and Hutchings 1977), would not have selected children with a biological family history of mental disorders.

### Oregon

Similar conditions existed in Oregon (Joseph 1999b, 2003), where the adoptees under study were placed between 1915 and 1945. Although unknown or unmentioned by Heston and most subsequent reviewers, in 1917 Oregon passed a law creating a State Board of Eugenics, whose duty was to authorize the compulsory sterilization of 'all feeble-minded, insane, epileptic, habitual criminals, moral degenerates and sexual perverts', because they might produce 'inferior' offspring (Olson 1920: 1487).

An additional 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 feeble-mindedness, insanity, epilepsy, criminality or degeneracy' (Olson 1920: 3176). Given that all of Heston's index adoptees were born to women hospitalized with schizophrenia, it is extremely unlikely that these children were placed into the same types of adoptive homes as the 'untainted' control adoptees (and many were placed in

foundling homes for several months or years). As twin researcher Einar Kringlen asked in relation to Heston's study, 'Because the adoptive parents evidently received information about the child's biological parents, one might wonder who would adopt such a child' (Kringlen 1987: 132–3).

### *Finland*

Finland also had a long history of eugenics-inspired legislation aimed at curbing the reproduction of 'hereditarily tainted' people. In 1935, the Finnish Parliament passed the Sterilization Act, which allowed the compulsory sterilization and castration of 'idiots,' 'imbeciles' and the 'insane', which included people diagnosed with schizophrenia and manic-depression (Hemminki *et al.* 1997; Hietala 1996).

In 1950, Finland passed the Castration Act, which permitted the compulsory castration of criminals, the mentally retarded and the 'permanently mentally ill'. It was not until 1970 that compulsory sterilization was legally abolished in Finland (Hietala 1996).

Because they began with diagnosed adoptees (as opposed to diagnosed biological parents), the studies of Kety *et al.* might appear less vulnerable to selective placement bias. However, in 8 of 33 index *adoptive* (rearing) families, a parent had been admitted to a Danish psychiatric facility, which was true for none of the 34 control adoptive families (Rose *et al.* 1984). This finding suggests that index adoptees were placed into more psychologically harmful adoptive homes than the control adoptees. Thus, the higher rate of spectrum diagnoses among index than control biological relatives might reflect little more than the agencies' placement of children with 'tainted' biological relatives into more psychologically harmful adoptive homes.

Thus, the crucial assumption that selective placement (on the basis of an adoptee's perceived genetic heritage) did not occur in the Danish, Finnish and Oregon adoption processes cannot be sustained. Like family and twin studies, the investigators were unable to control for environmental factors confounding the results of their studies. When we consider these studies' other serious methodological problems, there is little reason to accept their authors' conclusions about the role of genetics in schizophrenia.

## THE FUTILE SEARCH FOR SCHIZOPHRENIA GENES

The search for 'schizophrenia genes' has been underway for many years. The most common methods in molecular genetic research are linkage and association studies. In a linkage study, investigators look for genetic markers linked with the putative disease gene among consanguineous family members. Linkage studies are designed to identify areas of the

chromosome where relevant genes might be located, but they are unable to identify actual genes. Association studies compare the frequency of genetic markers among unrelated affected individuals and a control group.

The past few years have seen the publication of several studies claiming to have found a marker for a schizophrenia gene. Invariably, these studies fail attempts at replication. For example, Sherrington and colleagues' claim to have identified a marker in their 1988 *Nature* publication was accompanied by an article in the same issue by Kennedy *et al.*, who failed to replicate the findings. Nevertheless, it is widely believed that genes or genetic markers for schizophrenia and other psychiatric conditions have been found, when it is simply not the case.

In 1999, Williams and colleagues published a genome-wide schizophrenia linkage study that looked at 196 sibling pairs diagnosed with DSM-IV schizophrenia. While the investigators found some evidence 'suggestive' of linkage, 'none approached the genome-wide significance of 0.05'. Williams *et al.* concluded, 'Our results suggest that common genes of major effect . . . are unlikely to exist for schizophrenia' (p. 1729). In 2001, a study was published by Meyer and colleagues, who claimed to have found a significant association between a marker and catatonic schizophrenia. However, it is unlikely that these results will be replicated.

To date, molecular genetic studies have failed to find genes for schizophrenia. Most leaders of the field now believe that many genes are involved (the polygenic theory), and have abandoned the single-gene approach (Moldin and Gottesman 1997; Portin and Alanen 1997). In 2000, psychiatric geneticists Tsuang and Faraone wrote, 'We can now conclusively reject the idea that there is one gene of major effect that causes schizophrenia'. They recommended that future researchers should design studies 'to detect the many genes of small effect that each increase susceptibility to the disorder' (p. 1).

Although the failure to find schizophrenia genes does not prove that such genes do not exist, the belief that twin and adoption studies have already established the genetic basis of schizophrenia is erroneous. It is ironic that, instead of confirming the results of schizophrenia twin and adoption studies, the failure to find schizophrenia genes may well lead researchers to take a second look at these greatly flawed and environmentally confounded twin and adoption studies. Schizophrenia genetic researcher Lynn DeLisi has acknowledged that 'psychiatric genetics appears to be at a crossroads or crisis', as investigators continue to look for the 'elusive gene or genes' for schizophrenia (DeLisi 2000: 190). The 'crisis' facing psychiatric genetics is that investigators are looking for genes that probably do not exist.

Instead, psychiatric geneticists should undertake their own critical reanalysis of the original twin and adoption studies, which inspired the search for genes in the first place. In doing so, they will discover the reason that their search has turned up nothing. But suppose that they do even-

tually find something. One could still argue that, like phenylketonuria (PKU) and farsightedness, society's emphasis should be placed on environmental interventions. And researchers on all sides of the issue agree that environmental triggers are necessary to be diagnosed with schizophrenia.

## CONCLUSION

That the genetic basis of schizophrenia is a virtual proven fact in psychiatry speaks volumes about the discipline's failure to critically analyse the methods and assumptions of its own research. In countless textbooks in psychiatry, psychology and related fields, we find the same uncritical acceptance of the conclusions of twin and adoption researchers. Few textbooks present an accurate presentation of the evidence supporting the genetic position, and only a tiny handful attempt any kind of critical analysis (Joseph 2000b; Leo and Joseph 2002).

Moreover, genetic theories are very useful to the social and political elites' desire to locate the causes of psychological distress within people's bodies and minds, as opposed to their social environments. The widespread uncritical acceptance of the conclusions of schizophrenia twin and adoption researchers is an appalling development in the history of scientific research. It can be understood much more by psychiatry's interest in maintaining itself as a viable profession than on the basis of a careful review of the methods, assumptions and conclusions of the original studies.

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