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Editorial

Adoption Studies in Functional Psychosis

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Summary. The scientific rationale of the adoptive methods in genetic studies has been discussed. Three strategies have been employed in psychiatric research. In the adoptee's study method, one examines the adopted away offspring of biological parents, known to be affected by the disorder. A higher prevalence of the disorder among adoptees born to affected biological parents indicates that genetic factors are important. In the adoptee's relatives method, one starts with adoptees known to be disturbed, and then continues by investigating their biological and adoptive families. Comparisons of prevalence rates between relatives of the biological and the rearing index and control families permits one to estimate the influence of the genetic factors. A third method is cross-fostering, which is rarely employed. Children of normals who are "cross-fostered" to adoptive parents who later became ill, are studied. Adoption studies in the field of schizophrenia and manic depressive illness are more specifically discussed. Taken all together, the family, twin and adoption studies support the genetic etiology in schizophrenia and manic depressive illness, although it must be admitted that we need replications to arrive at firm conclusions in the last group of disorder.

Key words: Adoption studies – Functional psychosis – Twin studies – Schizophrenia – Manic depressive illness

Most mental illnesses run in the family. Is this due to genetic or social factors? Twin and adoption studies are best fitted to throw light on this complicated question.

Adoption studies might in theory prove the existence of inherited factors, because such studies are able to distinguish the effects of environment from the effects of genes. Resemblance between adopted-apart relatives reveals the impact of heredity, whereas similarities between adopted-together family members might indicate the importance of family environment. The transmitters of heredity and social experience can be separated because the biological parents are not the parents who reared the children. If schizophrenia is mainly genetically determined, one should expect adopted children of schizophrenic biological parents to suffer from schizophrenia nearly as frequently as children who grew up with their schizophrenic parents. On the other hand, if schizophrenia is largely socially transmitted, one would expect the frequency of schizophrenia in adopted offspring of schizophrenics to drop significantly.

A Historical Comment

The great interest in eugenics during the first part of this century also awakened an interest in adoption studies. Francis Galton (1822–1911), the famous cousin of Charles Darwin, developed some of the methods used today in the study of heredity: the family method, the twin method as well as statistical techniques to analyse the data. As early as 1875 he concluded: "There is no escape from the conclusion that nature prevails enormously over nurture when the differences in nurture do not exceed what is commonly to be found among persons of the same rank of society in the same country. My only fear is that my evidence seems to prove too much, and may be discredited on that account as it seems contrary to all expectation that nurture should go for so little" (Galton 1875); see also Cadoret (1986).

The 1940s and 1950s marked the beginning of adoption studies in mental disorder. Now the emphasis was on environmental factors, often to the exclusion of biological factors. The environmental bias was probably due both to the current zeitgeist, and to the greater accessibility of environmental information. It was much more difficult to obtain factual information about biological parents than about social parents. One exception was Roe's (1944) study of alcoholism.

Since the 1960s, interpretation of findings from adoption studies in psychiatry has mainly had a genetic bias. The most famous of these studies from this period are the Danish/American schizophrenia studies, carried out by Kety, Rosenthal and Wender, in collaboration with Schulsinger in Copenhagen. However, in recent years we have witnessed a series of adoption studies of alco-

holism (Goodwin et al. 1973; Cadoret et al. 1980; Cloninger et al. 1981), anti-social behaviour (Schulsinger 1977), somatization disorder (Sigvardson et al. 1984), affective disorder (Mendlewicz and Rainer 1977; von Knorring et al. 1983).

Strategy in Adoption Research

Three strategies have been employed in adoption studies.

In the *adoptee's study method* one can examine the adopted away offspring of biological parents known to be affected by the disorder. Or more specifically, the prevalence rates of the disorder among adoptees born to affected and non-affected parents are compared. A higher prevalence of the disorder among adoptees born to affected biological parents indicates that genetic factors are important and permits estimates of the heritability of the disorder. This method has been used by Heston (1966), Rosenthal et al. (1968) and Tienari (1991).

In the second method, *the adoptee's relatives study*, one starts with adoptees known to be disturbed, and then continues by investigating their biological and adoptive families. In addition, biological relatives of non-disturbed control adoptees are usually compared. Comparisons of prevalence rates between relatives of the biological and the rearing index and control families permits one to estimate the influence of the genetic factors. This design was used by Kety et al. (1968) in the study of schizophrenia, and by Mendlewicz and Rainer (1977) with regard to manic depressive illness. Comparisons of adoptive with biological relatives seem to reveal little because of the careful screening that has been common in adoption placements (Clerget-Darpoux et la. 1986).

A third method is the *cross-fostering method*, employed by Wender et al. (1974). This is a variation of the previous methods. Adoptees born to disturbed parents are compared with adoptees born to healthy parents, but reared by disturbed adoptive parents. In other words, these children of normals are "cross-fostered" to adoptive parents, who later become ill, for instance with schizophrenia.

The adoption study methods rest upon several important premisses, which might be questioned. Adoptees are not necessarily representative of the general population of non-adoptees with regard to the trait or illness that is studied. At least in Europe and North America, children who are adopted tend to be offspring of young, unmarried women. In addition, one cannot exclude that maternal age as well as circumstances regarding prenatal care, pregnancy and delivery could be related to the psychopathology under discussion. Furthermore, deficient diet, smoking and alcohol or substance abuse in the biological mother might affect the child to be adopted. Another assumption is that genes and social environment are uncorrelated with regard to factors that are relevant to the specific psychopathology. But just as selective placement may invalidate genetic influences, selective placement might also throw doubt on conclusions regarding environmental contributions. Secondly, as in most Western countries, the adoptive parents represent a restrictive range of environment for the adopted child (Kellmer-Pringle 1966). Usually adoptive parents are screened by the adoption agencies for health and socioeconomic status. Often also adoptive parents are older than parents in general. This narrowing of the range of variation in the adoptive home would decrease the correlations between environmental factors and psychopathology in the adoptees. Thirdly, most previous adoption studies show a correlation between socioeconomic status of the biological and that of the adoptive parents. Skodak and Skeels (1949) observed, for instance, that the children ending up in the better foster homes had biological mothers with higher IQs and more education. It is well known that "selective placement", defined as non-random placement of offspring in a home, takes place in the assignment of children to foster homes, particularly in terms of such variables as religion, family structure, values and child rearing practices. Often the staff members of private or public agencies seem to want to achieve some sort of fit between the child's background and its foster home. Finally, with regard to specific patient populations, for instance schizophrenia, the spouses of schizophrenics whose offspring are adopted tend to be more sick than such spouses in general. Hence, they are not representative of spouses of schizophrenics in general. It would appear that all of these weaknesses with regard to sampling lead to an over-estimation of genetic factors.

Schizophrenia

Adoptees' Study Method

Heston's (1966) pioneer study compared the psychosocial adjustment of 47 adults, born to schizophrenic mothers, with 50 matched controls of non-schizophrenic mothers. Five of 47 index subjects developed schizophrenia, versus none in the control group, thus strongly supporting a genetic hypothesis. However, not only schizophrenia, but sociopathic and neurotic behaviour as well as mental deficiency and artistic giftedness were found in greater excess than usual in the offspring born to schizophrenic mothers.

The conclusions drawn from the study might be questioned, because of several methodological problems. At the time of delivery the biological mothers were hospitalized for psychosis. The diagnoses of the mothers were exclusively based upon hospital records. Furthermore, because the adoptive parents evidently received information about the child's biological parents, one might wonder who would adopt such a child. In fact, most of the adoptive parents were paternal relatives. Heston's (1966) study also brings forth the problem of assortative mating, or the tendency toward non-random mating, which can affect the genetic condition in an adoption study. In this study, little was known of the biological fathers of the adoptees. The higher incidence of antisocial problems in the adopted away children could be the result of environmental factors. However, it could also have represented assortative mating of schizophrenic mothers with personality disordered fathers. Further-

more, the interviewer of the offspring was not blind as to who were index and who were control subjects.

Rosenthal et al. (1968) obtained a pool of 5483 adopted Copenhagen children and checked the names of their biological parents against the Danish psychosis register to acquire a sample of psychotic parents who had given their children up for adoption. Of the 76 parents originally selected, we are left with 52 with a diagnosis of schizophrenia, including 8 questionable cases.

Although the difference in psychopathology between adopted offspring of schizophrenics and of normal controls is not statistically significant at the 5% level, the figures are in accordance with a genetic hypothesis. Three offspring of schizophrenic parents (although only one had been hospitalized), as opposed to none of the offspring of the controls, were diagnosed as schizophrenic. The rate for hospitalized schizophrenia among the index adoptees is, however, remarkably low when compared with rates reported for offspring of schizophrenics in general. Rosenthal (1971) suggests that adoptive rearing may reduce the rate of schizophrenia because it is difficult to see how such a low rate could be explained by sampling bias.

Recently, the data have been subjected to blind reanalysis by Lowing et al. (1983). They included only identified biological parental pairs and index biological parents with the diagnosis of schizophrenia from the original series, using DSM-II criteria. A significant excess of schizophrenia spectrum was observed, comprising schizophrenia, schizotypal and schizoid personality (DSM-III) disorder in the adopted-away offspring of schizophrenic (15/39) versus control parents (5/39).

Rosenthal et al. (1975) did not obtain any social data directly from the adoptive parents, nor did they make any direct observation of adoptive family interaction. Their social data were limited to accounts from the adoptees when they were adults in which they described retrospectively their relationship with their adoptive parents. According to the reports of adoptees who had disturbed biological parents, the quality of their relationship with their adoptive parents was slightly worse than that described by adoptees with non-disturbed biological parents. Could it be that genetic factors for schizophrenia interfere with the shaping of behaviour by different rearing patterns (Rosenthal et al. 1975). One should also mention that in this study there was a positive correlation between the socioeconomic status of the adoptive father and the biological father; this indicates that some sort of selective placement had taken place.

The third and most comprehensive study with the adoptee's study method has been undertaken in Finland by Tienari et al. (1987, 1991). A sample of 288 adopted-away children of schizophrenic mothers have been compared with matched adopted controls, i.e. adoptees of non-schizophrenic biological parents. Whereas Rosenthal et al. (1968) studied the adoptive parents indirectly, Tienari and coworkers have investigated the adoptive families directly both with family and individual interviews and psychological tests.

Firstly, more subjects with severe mental disorders were observed in the offspring of schizophrenic mothers

Table 1. Outcome diagnoses of index versus control adoptees[a]

Adoptee diagnoses	Index adoptees			Control adoptees
	A	B	Total	Total
No diagnosis	62	5	67 (47.9%)	92 (57.7%)
Neurosis, mild personality disorder	27	4	31 (22.1%)	59 (33.1%)
„Soft-spectrum" non-psychotic personality disorder	25	4	29 (20.7%)	25 (14.0%)
Functional psychosis[b]	11	2	13 (9.3%)	2 (1.1%)

A, Confirmed RDC/DSM-III-R diagnoses of schizophrenia in biological mothers; B, including schizoaffective, schizophreniform, atypical and delusional psychoses

[a] Modified after Tienari (1991)

[b] Functional Psychosis: including total 8 (5.7%) DSM-III-R schizophrenia, 1 (0.7%) schizophreniform, 2 (1.4%) delusional disorder in index, and total 2 (1.1%) DSM-III-R schizophrenia in controls

than in the offspring of non-schizophrenic mothers. The diagnoses of the 140 index mothers are either schizophrenia, paranoid psychosis or atypical psychosis. As can be seen from Table 1, the offspring of index mothers are more frequently disturbed than the offspring of controls. Eight (5.7%) subjects with schizophrenia according to DSM-III-R were observed, compared with 2 (1.1%) subjects of 178 control adoptees.

Of considerable interest is the observation that severely disturbed adoptive families produce a large number of seriously disturbed individuals, if these are offspring of schizophrenic mothers. In healthy adoptive families little serious psychopathology was observed in either group. In both experimental and control groups, the mean rating of the offspring increases if the disturbance in the adoptive family becomes more severe. In other words, there is a clear-cut interaction of genetic and rearing factors. It is noteworthy that subjects with a genetic predisposition seem to be particularly vulnerable to a noxious family environment; likewise a healthy family milieu has probably protected genetically vulnerable children.

Critical Remarks

In the studies by Heston, Rosenthal and Tienari, the starting point was the schizphrenic mother who had given up her child for adoption. Based on family studies of schizophrenia, it is known that the risk of schizophrenia in offspring of schizophrenic parents is about 10%. The adoptive method makes it possible to discover whether the same risk persists when the children are separated from their schizophrenic parents and reared in another milieu. If such is the case, the genetic hypothesis is strongly correborated. One might ask, however, if these schizophrenic parents are representative of the general population of schizophrenics. Ninety percent of schizophrenics are born to non-schizophrenic parents, although some in addition have parents who are mentally disturbed. Could it be that the genetic contribution of schizophrenia is higher in that special group of schizophrenia?

Adoptees' Relatives Method

This strategy was used by Kety et al. (1968, 1975, 1978) in a study carried out in Denmark. They obtained a national sample of adoptees, but most of the published reports deal with the Copenhagen sample of 5483 adoptees, of whom 507 had been hospitalized for mental illness. On the basis of case summaries, the diagnosis of schizophrenia was established for 34, of whom 17 were chronic schizophrenics. Thirty-four control subjects consisted of carefully matched adoptees, who were not reported to the Central Psychosis Register. The Danish psychiatrist Bjørn Jacobsen interviewed personally nearly all the available relatives of indexes and controls. Afterwards these case notes were translated to English, and the American investigators performed a diagnostic review of the biological relatives.

As Table 2 shows, the biological relatives of schizophrenic adoptees include an excess of subjects with schizophrenia and uncertain schizophrenia, as opposed to the biological relatives of normal adoptees, and adoptive relatives who reared these adoptees. More specifically, when the 21 relatives with schizophrenic spectrum disorder were broken down in the various groups, 13 were biologically related to schizophrenic adoptees, and only 3 were biologically related to the control adoptees. These observations obviously support a genetic hypothesis of schizophrenia. The problem with these findings is, however, that the clear-cut difference is due to a very high frequency of schizophrenic spectrum disorder in the half-sibs. When comparing first-degree relatives (parents and full sibs), there is no difference between index and control families. Nine of the 13 biological relatives of the schizophrenic adoptees with a spectrum disorder were in fact half-sibs. If one compares only first-degree relatives in the groups of biological relatives of schizophrenics and biological relatives of normals, there are certainly more schizophrenic spectrum disorders in the index group (9/69, 13%) than in the control group (5/70, 7%), but the difference is not statistically significant. With regard to definite chronic schizophrenia, there is no difference at all, with 1 case in each group. This result is not remarkable, since the majority of first-degree relatives are parents in whom the prevalence is expected to be low. It does, of course, weaken the genetic hypothesis.

In order to strengthen the validity of these findings, psychiatric interviews of the biological and adoptive relatives were carried out by a Danish psychiatrist who did not know to which group they belonged. A significantly greater frequency of schizophrenic spectrum disorders occurred among the adoptive relatives of the schizophrenic adoptees (Kety et al. 1975). Of the biological relatives of the 173 index cases, 37 (21.4%) received a schizophrenia spectrum diagnosis, compared with 19 (10,9%) of the 174 controls (but again, first- and second-degree relatives have been lumped together).

Kendler and Gruenberg (1984) re-analysed the data employing the DSM-III criteria and reported a higher rate of schizophrenia spectrum in first-degree versus second-degree biological relatives of schizophrenic adoptees (4/10 or 40% versus 5/25 or 20%), and significantly higher rates of schizophrenic spectrum disorders in biological relatives of schizophrenics compared with control-adoptees, considering either first-degree or second-degree relatives only. However, the numbers are small. Out of a total of 34 schizophrenic adoptees, only 13 met DSM-III criteria of schizophrenia. These 13 index adoptees had 35 biological relatives; this included first- and second-degree relatives, but only 10 first-degree biological relatives. Of these 10 first-degree biological relatives, 1 was schizophrenic, 2 schizotypal and 1 had a paranoid personality disorder.

Table 2. Schizophrenic-like disorders in biological and adoptive relatives of schizophrenic and normal adoptees in Kety's study: records and interview data

Category	Total	Definite or uncertain schizophrenia	
		n	%
Biological parents			
of schizophrenic adoptees	66	8	12.1
of control adoptees	65	4	6.2
Adoptive parents			
of schizophrenic adoptees	63	1	1.6
of control adoptees	68	3	4.4
Biological half-sibs			
of schizophrenic adoptees	104	19	18.3
of control adoptees	104	3	2.9

In this connection one should also mention Kinney and Jacobsen (1981), who studied schizophrenic adoptees without a genetically presumed liability to the disorder (the Kety study). Schizophrenic individuals who had a biological parent, sibling or half-sibling diagnosed as having schizophrenia were compared with schizophrenics without such relatives. Certain environmental variables were studied, including personality traits of the adoptive parents noted at the time they were interviewed. These authors hypothesized that environmental factors which contributed to schizophrenia would be more severe for individuals who become schizophrenic with presumed low genetic vulnerability. According to the study, the adoptive parents with a low "genetic" liability to schizophrenia had been more shy and reserved as adults, more restricted and non-spontaneous, having had more phobias as adults, and in addition they had been more frequently teased as children and had performed poorly in school. Such traits, which are more typical of parents of low genetic liability, might provide some support for the hypothesis that psychosocial environmental factors contribute to development of schizophrenia. In addition, more pregnancy and birth complications in schizophrenic adoptees were observed compared with matched controls.

Critical remarks

It is somewhat unclear how Kety, Rosenthal and Wender arrived at their diagnosis, and no information was given about reliability. Also the researchers obviously

changed their criteria of schizophrenia spectrum during the diagnostic process. Lidz et al. (1981) maintained that several index adoptees should not have been included in the sample. With a smaller sample size, there would be no significant differences at all between biological relatives of schizophrenic adoptees and controls. However, later independent analysis of the data with DSM-III criteria has in the main come to the same conclusions as the original studies (Kendler et al. 1981; Kendler and Gruenberg 1984). Not all critiques are, however, satisfied. Rose et al. (1984) reported, for instance, that one subject – a biological relative of an index subject – had twice been given the diagnosis of manic depressive illness by hospital doctors. Later she received the diagnosis of uncertain borderline schizophrenia/severely schizoid personality, based on an interview. The fact seems to be, however, that the woman had never been interviewed. The psychiatrist responsible for the interviews had made up an interview from her hospital notes.

In their analysis Kety et al. combine first- and second-degree relatives as "biological relatives". This has been criticized (Benjamin 1976; Gottesman and Shields 1976; Kringlen 1976). First-degree relatives have 50% of their genes in common with the probands (parents and children have exactly 50% of their genes in common with the probands, while sibs on the average have 50%). Second-degree relatives average only 25% of the genes in common. Genetic theory would, of course, predict that the prevalence in half-sibs was considerably lower than in the first-degree relatives. The pooled risk in full siblings is usually around 8–10%, and 3–4% in half-sibs.

In their 1975 report, Kety and coworkers showed a separate analysis for biological paternal half-sibs. There was a significantly higher rate of spectrum diagnosis among the paternal half-sibs of index adoptees than among paternal half-sibs of controls. The high half-sibling rate could not be accounted for by intra-uterine, perinatal or early post-natal maternal factors, since the rate was even higher for the paternal half-sibling than for the maternal half-sibs. However, the frequency of spectrum diagnosis does not differ between maternal half-sibs of the index and control subjects. Thus the higher rates of schizophrenia spectrum in the paternal half-sibs can only be explained by psychosocial factors or by chance.

Manic and Depressive Conditions

Adoption studies in the field of affective disorder are few, and only one method has been employed: the adoptees' relatives method, based on the study of biological relatives of adoptees with affective disorder.

In a study from Belgium, Mendlewicz and Rainer (1977) observed more psychopathology of an affective kind in the biological relatives of adoptees with bipolar illness, compared with social relatives in the adoptive families.

The group of manic depressive adoptees was established by systemically examining the medical records of five outpatient and five inpatient services in the vicinity of Brussels during a 5-year period (1971–1976). The diagnosis was confirmed by semistructured interviews and only persons who had experienced both manic and depressive episodes were included in the sample. Three sets of controls were obtained, namely parents of manic depressives who were not adopted, adoptive and biological parents of normal adoptees, and parents of individuals who had contracted poliomyelitis during their younger years.

Table 3. Diagnosis of parents of bipolar and normal adoptees[a]

Diagnosis	Bipolar adoptees ($n = 29$)		Normal adoptees ($n = 22$)	
	Biological parents	Adoptive parents	Biological parents	Adoptive parents
Bipolar	4	1	0	0
Unipolar	12	6	1	3
Schizoaffective	2	0	0	0
Cyclothymic	0	0	0	1
	18 (31%)	7 (12%)	1 (2%)	43 (10%)
Schizophrenia	0	0	0	1
Alcoholism	3	2	3	0
Sociopathy	2	0	3	0
Other	0	0	1	0
	23 (40%)	9 (16%)	8 (18%)	5 (11%)

[a] Modified after Mendlewicz and Rainer (1977)

The major findings of this study was that affective psychopathology in the biological parents was in excess of that found in the adoptive parents of the same manic depressive offspring. The difference is statistically significant if one compares the total affective spectrum, i.e. bipolar cases, unipolar cases (psychotic depression without mania), schizoaffective psychosis and cyclothymia.

More specifically, affective disorder including so-called spectrum disorder was found in 31% of the biological parents, compared with 12% of the adoptive parents of 29 bipolar adoptee probands. The morbid risk in biological parents was comparable to the risk found in parents of non-adoptive bipolar patients, and higher than biological or adoptive parents of normal adoptees.

The greater degree of psychopathology, particularly affective disorders in parents genetically related to the manic depressive probands, compared with parents who had adopted and raised the same individuals, shows the importance of genetic factors in the aetiology of manic depressive illness. However, as regards bipolar disorder, although the number of bipolar cases is higher in the biological parents than in the adoptive parents as well as in the parents of controls, the difference is not statistically significant at the 5% level.

In this Belgian study, the majority of affected biological parents suffered from a unipolar and not a bipolar disorder. This finding might indicate that these two conditions are not separate illnesses. One should, of course, also take into account the base rate of the two conditions, unipolar conditions being much more frequent.

In an adoption study from Sweden by von Knorring et al. (1983), there was no increase in affective psychopathology in biological parents compared with adoptive parents of adoptees with affective disorder. Indirectly these authors substantiated the significance of the family environment for the transmission of depression in the family. Thus a stronger relation between depression in adoptees and their social parents was observed than between the adoptees and their biological parents. Of the total sample of 56 cases with affective disorder, 40 had non-psychotic depression and 16 had affective psychosis. Five of the 98 biological parents (mothers and fathers) had been treated for an affective disorder, i.e. 5.1%. However, healthy adoptees had approximately the same percentage of biological parents with an affective disorder, namely 5.4% (11/203).

The important finding here is the excess of affective psychosis in the social parents. As the authors themselves point out, such cases were likely to be reliably ascertained by the case-finding method employed.

It is also of great interest that there was no significant concordance between the specific diagnosis of the biological parents and their adopted children. Subdivisions of depressive patients according to the dichotomies psychotic/non-psychotic and reactive/non-reactive did not yield subgroups with distinct family histories.

At first, one might think that these two studies are at variance with each other. However, this is only apparent. The Belgian study focused attention on bipolar pathology and strongly supports the twin studies. The Swedish study concentrated, however, on lighter and moderately severe depression, in which twin studies have shown that the genetic component is rather weak. Thus all in all, these two studies support the findings from twin studies.

Recently Wender et al. (1986) studied biological relatives of adoptees with affective disorder in Denmark. The investigators include unipolar, bipolar and uncertain cases of major mood disorders as one subgroup, and neurotic depression and affective reaction as another. Together the two subgroups are designated broad affective spectrum, with the first subgroup as "hard affective spectrum". They observed 71 relatives of bipolar adoptees, and 132 relatives of unipolar adoptees with 4.2% and 5.3% hard affective spectrum diagnosis respectively. These rates are higher than the 2.3% among the 313 controls. However, the difference is not statistically significant. It is also noteworthy that these rates are lower than those usually found in family studies. Whether this was due to the fact that information was obtained exclusively from medical records without direct access to family history is unclear. Anyhow, this study does not provide strong support for hereditary factors in these disorders.

In this connection I would briefly like to mention one adoption study of suicide. Although severe affective depression is only one important cause of suicide, adoption studies might throw light on aetiological problems. In a Danish study, a considerably higher suicide rate was observed in biological relatives of adoptees with affective disorder. Fifteen of 381 (3.9%) biological relatives of 71 adoptees with affective disorder had committed suicide, compared with 1 out of 168 (0.6%) adoptive relatives of adoptees with affective disorder (Schulsinger et al. 1989; Wender et al. 1986).

Conclusion

The adoption design is one of the most powerful methods in the study of nature/nurture. However, as I have attempted to show, adoption studies in functional psychosis have their limitations. There are sources of error, and the findings are liable to various interpretations, because of diagnostic uncertainty, small numbers without significant statistical differences, disputable analysis of data, and doubt with regard to generalizability.

Nevertheless, taken all together, the family, twin and adoption studies, in my view, support a genetic aetiology in schizophrenia. With regard to manic and major depression, both twin and adoption studies based upon population sampling are rare. Only one large adoption study supports the findings from twin studies to the effect that bipolar disorder is highly inheritable. Obviously, we need replication to arrive at firm conclusions.

References

Benjamin LS (1976) A reconsideration of the Kety and associates' study of genetic factors in the transmission of schizophrenia. Am J Psychiatry 113:1129–1133

Cadoret RJ (1986) Adoption studies: historical and methodological critique. Psychiatr Dev 1:45–64

Cadoret RJ, Cain C, Growe RR (1980) Development of alcoholism in adoptees, raised apart from alcoholic biological relatives. Arch Gen Psychiatry 37:561–563

Clerget-Darpoux F, Goldin LR, Gershob ES (1986) Clinical methods in psychiatric genetics. III. Environmental stratification may simulate a genetic effect in adoption studies. Acta Psychiatr Scand 74:305–311

Cloninger CK, Bohman M, Sigvardsson S (1981) Inheritance of alcohol abuse, cross-fostering analysis of adopted men. Arch Gen Psychiatry 38:861–868

Galton F (1875) Cited after Cadoret R (1986) Adoption studies: historical and methodological critique. Psychiatr Dev 1:45–64

Goodwin DW, Schulsinger F, Hermansen L (1973) Alcohol problems in adoptees raised apart from alcoholic biological parents. Arch Gen Psychiatr 28:238–243

Gottesman II, Shields J (1976) A critiqual review on recent adoption, twin and family studies of schizophrenia: behavioral genetic prospectives. Schizophr Bull 2:360–401

Heston LL (1966) Psychiatric disorders in foster home reared children of schizophrenic mothers. Br J Psychiatry 112:819–825

Kellmer-Pringle MT (1966) Adoption – facts and fallacies. Longmann, London

Kendler KS, Gruenberg AM (1984) An independent analysis of the Danish adoption study on schizophrenia. VI. The relationship between psychiatric disorders as defined by DSM-III and the relatives and adoptees. Arch Gen Psychiatry 41:555–564

Kendler KS, Gruenberg AN, Strauss JS (1981) An independent analysis of the Copenhagen sample of the Danish adoption study of schizophrenia. II. The relationship between schizotypal personality disorder and schizophrenia. Arch Gen Psychiatry 38:982–984

Kety SS, Rosenthal D, Wender R, Schulsinger F (1968) The types and prevalence of mental illness in the biological and adoptive families of adopted schizophrenics. In: Rosenthal D, Kety SS

(eds) The transmission of schizophrenia. Pergamon Press, New York, pp 345–362

Kety SS, Rosenthal D, Wender PH, Schulsinger F (1975) Mental illness in the biological and adoptive families of adoptive individuals who have become schizophrenic. In: Fieve RR, Rosenthal D, Brill H (eds) Genetic research in psychiatry. Johns Hopkins University Press, Baltimore, pp 111–120

Kety SS, Rosenthal D, Wender PH, Schulsinger F, Jacobsen B (1978) The biological and adoptive families of adopted individuals who became schizophrenic: prevalence of mental illness and other characteristics. In: Wynne LC, Cromwell RL, Mathysse S (eds) The nature of schizophrenia. Wiley, New York, pp 25–37

Kinney DK, Jacobsen B (1981) Environmental factors elucidated by adoption studies. In: Perris C, Struwe G, Jansson B (eds) Biological psychiatry, Elsevier, Amsterdam

Knorring AL von, Cloninger CR, Bohman M, Sigvardsson S (1983) An adoption study of depressive disorder and substance abuse. Arch Gen Psychiatry 40:943–950

Kringlen E (1976) Twins – still our best method. Schizophr Bull 2:429–433

Lidz T, Blatt S, Cook B (1981) Critique of the Danish/American studies of the adopted-way offspring of schizophrenic parents. Am J Psychiatry 138:1063–1068

Lowing PA, Mirsky AF, Pereira R (1983) The inheritance of schizophrenia spectrum disorders: a re-analysis of the Danish adoptee study data. Am J Psychiatry 140:1167–1171

Mendlewicz J, Rainer J (1977) Adoption study supporting genetic transmission in manic depressive illness. Nature 268:327–329

Roe A (1944) Adult adjustment of children of alcoholic parents raised in foster homes. Q J Stud Alcohol 5:378–393

Rose S, Kamin LJ, Lewontin RC (1984) Not in our genes. Penguin, London

Rosenthal D (1971) Two adoption studies of heredity in the schizophrenic disorders. In: Bleuler M, Angst J (eds) Die Entstehung der Schizophrenie. Huber, Bern, pp 21–34

Rosenthal D, Wender PH, Kety SS, Schulsinger F, Welner J, Østergaard L (1968) Schizophrenic offspring reared in adoptive homes. In: Rosenthal D, Kety SS (eds) The transmission of schizophrenia. Pergamon Press, New York, pp 377–392

Rosenthal D, Wender PH, Kety SS, Schulsinger F, Welner J, Riedker (1975) Parent-child relationships and psychopathological disorder in the child. Arch Gen Psychiatry 32:466–476

Schulsinger F (1977) Psychopathy. Heredity and environment. In: Mednick SA, Christiansen KO (eds) Biosocial basis of criminal behavior. Gardner Press, New York

Schulsinger F, Kety SS, Rosenthal D, Wender PH (1979) A family study of suicide. In: Schou M, Strømgren E (eds) Origin: prevention and treatment of affective disorders. Academic Press, London

Sigvardsson S, Knorring AL von, Bohman M, Cloninger CR (1984) An adoption study of somatoform disorders. I. The relationship of somatization to psychiatric disability. Arch Gen Psychiatry 41:853–858

Skodak M, Skeel HM (1949) A final follow-up study of one hundred adopted children. J Genet Psychol 75:85–125

Tienari P, Sorri A, Lahti I et al (1987) Genetic and psychosocial factors in schizophrenia: the Finnish adoptive family study. Schizophr Bull 13:477–484

Tienari P (1991) Genes, family environment or interaction. Findings from an adoption study. In: Kringlen E, Lavik NJ, Torgersen S (eds) Etiology of mental disorder. Department of Psychiatry, University of Oslo, pp 25–35

Wender PH, Rosenthal D, Schulsinger F, Jacobsen B (1974) Cross-fostering – a research strategy for clarifying the role of genetic and experimental factors in the etiology of schizophrenia. Arch Gen Psychiatry 30:121–128

Wender PH, Kety SS, Rosenthal D, Schulsinger F, Ortmann J, Lunde L (1986) Psychiatric disorders in the biological and adoptive families of adopted individuals with affective disorders. Arch Gen Psychiatry 43:923–929