Is There an Increase of Reproductive Rates in Schizophrenics?

I. Critical Review of the Literature *

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Summary. It is well-known that the fertility of schizophrenic patients, particularly males, is below the population average. The main measures of fertility (reproductivity) are marriage rate, marital fertility, and rate of reproduction. A review of the literature reveals the rate of reproduction of schizophrenic patients to be 30% to 80% of the general population, the reduction being mainly due to reduced probability of marriage. At least one investigation presented evidence for an increase in marriage rate and rate of reproduction in schizophrenic patients relative to the general population in recent time. If this increase were to be confirmed it would undoubtedly have practical as well as theoretical implications. The hypothesis of a compensatory higher fertility of healthy relatives of schizophrenics based on a physiological advantage is empirically unproven. Additionally, the concept of a balanced polymorphism in schizophrenia rests on a superficial analogy with Mendelian traits.

Key words: Fertility – Schizophrenia – Reproductive rates – Selective advantage

Zusammenfassung. Seit langem ist bekannt, daß Schizophrene, besonders männliche Patienten, eine gegenüber der Allgemeinbevölkerung herabgesetzte Fertilität haben. Die wichtigsten Meßgrößen der Fertilität sind die Heiratsrate, die eheliche Fertilität und die allgemeine Rate der Reproduktivität. In der Literatur liegt die allgemeine Rate der Reproduktivität schizophrener Patienten bei 30–80% der Allgemeinbevölkerung. Dies beruht in erster Linie auf einer herabgesetzten Heiratsrate. Eine Studie beschreibt eine Angleichung der Heiratsrate und der allgemeinen Reproduktivität von schizophrenen Patienten an die Allgemeinbevölkerung. Wenn der Anstieg sich bestätigen ließe, dann wäre dies von theoretischer und praktischer

Bedeutung. Für die Hypothese einer kompensatorisch erhöhten Fertilität der gesunden Verwandten von Schizophrenen, die sogar mit einem physiologischen Vorteil in Zusammenhang gebracht worden ist, gibt es bislang keine empirischen Belege. Das Konzept eines balancierten genetischen Polymorphismus bei der Schizophrenie beruht auf einer oberflächlichen Analogie mit Mendelschen Merkmalen.

Schlüsselwörter: Fertilität – Schizophrenie – Reproduktivität – Selektionsvorteil

Introduction

Fertility[1] of psychiatric patients, particularly schizophrenics, has been of continuous interest for the last 80 years. During the early decades of this century, the motivation for the interest in this problem was the eugenics paradigm. Supported by the exciting discoveries of evolutionary processes and the progress in the field of genetics, the fear predominated among many scientists that overproportional reproductive rates of mentally ill people would lead to a deterioration of the human species. This belief was particularly based on the opinion that psychiatric diseases such as schizophrenia were inherited in a Mendelian way. Looking back, the eugenics movement obviously applied Mendel's laws in an oversimplified and uncritical way to mental traits. Today, a polygenic theory of schizophrenia (Gottesmann and Shields 1967) is usually favoured: the disorder is treated as a threshold character whose phenotypic appearance depends on both the number of genes present and the amount of stress. Polygenic models, however, are very general and therefore unsatisfactory, because they tell little about the nature of the responsible genes. In addition, genetic heterogeneity of schizophrenia has to be taken into account, as e.g. in mental retardation (Zellweger and Jonasescu 1978) and in epilepsy (Newmark and Penry 1980). There are a number of findings that strongly support the concept of etiologic heterogeneity in schizophrenia (Reid 1973; Vogel and Propping 1982).

The problem of fertility of schizophrenics remains mainly for two reasons: a theoretical and a practical one.

The theoretical problem is the rather stable prevalence of schizophrenia in the population in spite of the fact that schizophrenic patients have markedly reduced reproductive rates as compared to the general population. The practical problem concerns the genetic and social consequences for the children of schizophrenics. This aspect attracted growing general interest in the last decade since Erlenmeyer-Kimling et al. (1969) published an increase in reproductive rates of schizophrenics in recent times relative to the normal population. If this finding reflected a general tendency, it would undoubtedly have practical importance.

Approximately 10% to 15% of the children of a schizophrenic are expected to develop a comparable psychosis (Zerbin-Rüdin 1980). If the reproductive rate of schizophrenics increases, the number of persons at risk in the next generation

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1 In this review the terms "fertility" and "reproductivity" will be used interchangeably, and exclusively in the demographic sense

would also increase. Therefore, this aspect is of practical importance for preventive medicine. In another disease with an obvious genetic basis—Huntington's chorea—the number of persons at risk in a population is being monitored in epidemiological surveys as in south Wales (Harper et al. 1979). In this case, it is possible to determine the frequency of detrimental genes in the population. Interestingly, there is—presumably as a consequence of genetic counselling—a pronounced fall in the number of births at risk for Huntington's chorea and in the predicted future incidence of the disease (Harper et al. 1981).

In addition, a child living with a mentally disturbed parent may experience distress. The adult person may therefore bear lifetime scars due to emotional traumas during childhood. The familial situation has to be regarded as particularly burdened when the spouse of a schizophrenic parent also suffers from a psychiatric disorder. When a wide range of mental problems is included, several studies showed a remarkable degree of assortative mating although the diagnostic homotypia is usually low (Erlenmeyer-Kimling et al. 1978). Fowler and Tsuang (1975) evaluated spouses of schizophrenics on the basis of psychiatric interviews and reported that 39% of them were psychiatrically disturbed. Over 50% of ever-married schizophrenic patients are divorced or permanently separated from their spouses (Bleuler 1972; Erlenmeyer-Kimling et al. 1978). All these complications together in families of schizophrenics may trigger unfavourable developments in the life of their children, even if they do not become schizophrenic. In his nearly life-long study on schizophrenics Bleuler (1972) assessed the home conditions in which the children of schizophrenics grew up: the conditions were only "favourable" in approximately 20%, whereas they were "horrible" in nearly 20%, at least during essential periods of the child's development. For the patient, on the other hand, as Ødegard (1960) formulated, the responsibility for a family may frequently be an obstacle on the road towards social rehabilitation.

For all these reasons there would be practical implications if the reproductive rate of schizophrenic patients had in fact been increasing in recent time. Before presenting the results of an own investigation on this problem we shall critically review the main data from the literature.

1. Studies Comparing Reproductive Rates of Schizophrenics and Normals

Measures of reproductive performance of the patients have to be related to the general population. In accordance with Ødegard (1960), we tried to extract the following rates from the literature:

marriage rate = no. of patients married per 100 expected,
marital fertility = no. of children of married patients per 100 expected,
rate of reproduction = no. of children of the patients per 100 expected ("fitness").

When only marital fertility is taken into account, the rate of reproduction should be the product of marriage rate and marital fertility.

Table 1 summarizes the studies performed on fertility of schizophrenics. We will briefly comment on the methodological factors that may have influenced the results.

Table 1. List of the main investigations on fertility in schizophrenics. Marriage rate = no. of rate of reproduction = no. of children per 100 expected

Authors	Case definition	No. of cases	Period of admission	Follow-up period
Essen-Møller (1935, 1936)	Psychiatric inpatients, clinical diagnosis	1194	1904–1927	Until Jan. 1st, 1931
Kallmann (1938)	Clinical diagnosis, manifest schizo-phrenia before the age of 40	1087	1893–1902	1929–1937
Böök (1953)	Personal diagnosis	85	1902–1949	1949
Garrone (1962)	Clinical diagnosis	60 fem.	1940–1950	---
MacSorley (1964)	Clinical diagnosis	77 fem., 78 males	1958–1960	---
Stevens (1969)	Clinical diagnosis, all female schizo-phrenics, aged 16–49 years, ad-mitted for the first time to one hospital	811	1955–1963	Until August 31st, 1965
Lindelius (1970)	Clinical diagnosis, mostly first-ever admis-sions	270	1900–1910	1960's
Slater et al. (1971)	Clinical diagnosis	2089	1952–1966	---
Bleuler (1972)	Personal diagnosis	108 fem. 100 males	1942–1943	Until 1965

patients married per 100 expected, marital fertility = no. of marital children per 100 expected,

Controls	Marriage rate	Marital fertility	Rate of reproduction
960 marriages in Munich (1876–1930) and 279 uncles and aunts of traumatic epileptics	Prepsychotic 50, postpsychotic 15	Marriage before disease onset: <100, particularly postpsych.; marriage after onset: 100	30–40
German data from Muckermann, 1931, and census data, no control for age	56 for the hebephrenic-catatonic group, 107 for the paranoid-simplex group	100 paranoid, 54 hebephrenic and catatonic, ♂ = ♀	
Matched controls from the same area	78 for females, 31 for males	>100	70
Census data	<100	36 for females	
2 sets of controls: census data and a local sample of normals	49 for females, 63 for males	61 for females, 80 for males	
Census data matched for age at marriage and duration of marriage	73 before first admission, 36 after first admission	88 before first admission, 71 after first admission	
Census data from 1930	56 for females, 34 for males	94 before onset, 80 after onset	37
National census data	≪100	73 for both sexes	≪100
Estimates from census data	≪100	100 for females, 50 for males (est.)	50 (est.)

Table 1 (continued)

Authors	Case definition	No. of cases	Period of admission	Follow-up period
Vogel (1979)	Inpatients of a univ. clinic, diagnosis according AMP	708	1968–1975	---
Burr et al. (1979)	Standardized diagnosis according Diagno III-M, only outpatients	223 fem., $3/4$ of whom are black	Jan.–June of 1976	---
Huber et al. (1979)	Personal diagnosis acc. K. Schneider	502 (66% first admissions)	1945–1959	1967–1973
Lavik (1982)	Inpatient census and psychiatric referrals	57 fem., 61 males	1979	---

Diagnosis. In most studies the investigator had to rely on the clinical diagnosis. Only the newer studies by Vogel (1979) and Burr (1979) were based on standardized psychiatric criteria. At least some of the differences in the results between the studies will be accounted for by diagnosis.

Case Definition. This is one of the most crucial points. If all the hospitalized patients irrespective of their numbers of individual admissions are taken into account, this will lead to an overrepresentation of the cases with multiple hospitalizations. If a clinic does not have a defined catchment area as is usually the case for university hospitals there will be a selection of certain patients. Most studies are restricted to inpatients. Sometimes, however, outpatients who will usually show less severe courses of the disease were also included. These problems can only be solved by a case definition on epidemiological grounds.

A selection for multiple admissions has to be taken for granted in all studies except those by Böök (1953), Stevens (1969), and Lindelius (1970). Böök succeeded in a complete ascertainment of all schizophrenics of a restricted region. Stevens and Lindelius defined their cases as first-ever admissions, respectively. The index cases of Slater et al. (1971) included inpatients and outpatients, whereas Burr et al. (1979) examined only outpatients. Outpatients will a priori exhibit a smaller reproductive deficit than inpatients.

Marital Status. Marriage has of course an important influence on reproductivity. Varying proportions of married individuals among the patients may therefore contribute to different fertility rates between studies.

Controls	Marriage rate	Marital fertility	Rate of reproduction
National census data matched for age and duration of marriage	≪100	65	36
300 females from a fertility survey in the same region	---	(100)	(85)
---	≪100	<100	
Census data from the catchment area, no control for age	54 for females, 24 for males		

Essen-Møller (1935) discovered an overrepresentation of widowed patients in his material. For calculations of the probability of marriage, he therefore corrected the number of married patients. Since this procedure was presumably overdone, marriage and fertility data were later corrected (Essen-Møller 1936). Böök (1953) observed among his patients an unusually high proportion of married females as a consequence of the shortage of young females in the isolated region. A reinvestigation confirmed the still high marital fertility, although the percentage of all reproducing female schizophrenics, married and unmarried, had declined from 73% in 1949 to 48% in 1977 (Modrzewska 1980).

Duration of Follow-up. The studies differ as to the duration of the follow-up period during which fertility of the patients was determined (Table 1). In some investigations the complete fertile period is evaluated (e.g. Kallmann 1938; Garrone 1962; Lindelius 1970), whereas in others reproductivity is determined only up to hospital admission (Slater et al. 1971; Vogel 1979). A distinction between pre- and postpsychotic fertility was only made by some authors (e.g. Stevens 1969).

Control Data. The origin of the control data is one of the most crucial points, and in the majority of studies, census data were used for comparison (Table 1). Because of a questionable comparability with respect to social class, town-country relationship, or even age structure and marital status, such a procedure is however problematic. Individual matching of controls will lead to better comparability.

Table 2. List of the investigations which examined the problem of changing fertility

Authors	Case definition	No. of cases	Period of admission	Follow-up period
Ødegard (1960)	Clinical diagnosis, first-ever admissions	All married schizo-phrenics among 3002 females and 2762 males	1936–1945	---
	Clinical diagnosis, first-ever admissions	All married schizo-phrenics among 4229 females and 3641 males	1946–1955	---
Erlenmeyer-Kimling et al. (1969) Goldfarb and Erlenmeyer-Kimling (1962)	Clinical diagnosis, controlled according APA crite-ria, all hos-pital admis-sions	1118, of whom 976 survived follow-up	1934–1936	Dec. 31, 1941
	Clinical diagnosis, controlled according APA crite-ria, all hos-pital admis-sions	781, of whom 705 survived follow-up	1954–1956	Dec. 31, 1961
Shearer et al. (1968)	All psychiatric cases	Estimated: 8728	1935–1964	---

2. Studies Examining a Possible Increase of Reproductive Rates

Essen-Møller (1935) had already reported that under conditions of decreasing general birth rates as in the first decades of this century, fertility of schizophrenics, at least in males, lags behind the population trend. Ødegard (1960) was the first to directly examine the problem of a possible relative increase of reproductive rates in schizophrenics. In his as well as in the other studies on this problem, the same methodological aspects as mentioned previously have to be considered.

Ødegard (1960) analyzed the data from the Norwegian national register of mental disorder. He examined marriage and fertility rates at the time of first-ever admission of a patient. Whereas the census data gave fertility rates for normal females, Ødegard had to estimate indirectly the respective rates for males. The

rates in schizophrenics

Controls	Marriage rate	Marital fertility	Rate of reproduction
National census data from 1920, 1930, 1946 and 1950. Control for age and duration of marriage	49.2 for females, 39.5 for males; only pre-psychotic	89.7 for females, 80.9 for males; only pre-psychotic	44.1 for females, 32.0 for males
	56.6 for females, 37.5 for males; only pre-psychotic	93.3 for females, 104.4 for males; only pre-psychotic	52.8 for females, 39.2 for males
Birth cohort data from US Vital Statistics, Control for age	78 for females, 38 for males	100 for females and males	58 for females at admission, 46 for females at follow-up
	82 for females, 47 for males	100 for females and males	70 for females at admission, 54 for females at follow-up
Census data, no control for age	Not given	Not given	Not given

authors observed slight increases of marital fertility and total reproductivity between the two periods in the schizophrenics as compared to the normal population (Table 2). This increase, however, cannot be due to influence of treatment, because the data refer to the time before first admission.

Ødegard (1980) continued his investigation on fertility of psychiatric patients, and again observed a slight increase of marital fertility in psychiatric patients as compared to census data, however, without differentiating the diagnoses.

The study by Erlenmeyer-Kimling et al. (1969) on changes in fertility rates of schizophrenic patients can be regarded as a milestone in the series of investigations on this problem. These authors compared the demographic parameters relevant for reproduction in two cohorts of schizophrenic patients admitted to New York State hospitals (Table 2).

The two samples were drawn from all patients admitted to 11 psychiatric hospitals. In order to correct for multiple admissions the authors weighted every case by dividing its initial probability of selection by the number of hospital admissions during the sampling period. They observed a lessening of the differential between the schizophrenic and the general population cohorts in the later as compared to the earlier sample, both at survey admission and after 7 years of follow-up. Their interpretation is that as a consequence of changing attitudes of society toward psychiatric patients and particularly the abbreviation of hospital stay, a gain in reproductive performance was favoured in schizophrenic patients.

Shearer et al. (1968) reported an increase of 355% in the birth rate within Michigan's major state mental hospitals. The authors attributed this effect to an "open door" policy practiced in psychiatric institutions. For methodological reasons, however, the outcome of the study is not tenable.

3. The Question of Reproductive Compensation by Relatives

The problem how the stable incidence and prevalence rates of schizophrenics in the population are achieved in spite of the obvious reduction of their fertility has been of interest for decades. Since schizophrenia has an hereditary component, different mechanisms such as mutation, physiological advantage, disease resistance, or reproductive compensation by relatives have been hypothesized. If only few genetic loci were implicated in the genetic determination of schizophrenia, the required mutation rate would be much higher than any known. Concepts about physiological advantages remained speculative (e.g. Jarvik and Deckard 1977), and so far no disease is known that effects schizophrenics less than non-schizophrenics.

The hypothesis of reproductive compensation by relatives was favoured by Erlenmeyer-Kimling and Paradowski (1966) who suggested evidence for slightly increased fertility of the healthy siblings of schizophrenics. This finding aroused widespread interest because of the parallel with the well-known selective heterozygote advantage in sickle cell anemia. The empirical examination of this hypothesis, hoowever, failed to yield any proof for a higher fertility of the relatives of schizophrenic patients. The most careful study was that of Buck et al. (1975) who compared reproductive rates of 1195 siblings of schizophrenics with census data of the general population allowing for sex, age at marriage and duration of marriage. The same negative results were obtained by Lindelius (1970), Rimmer and Jacobson (1976), Vogel (1979), and Essen-Møller (1936), who examined fertility of either the siblings or the parents of schizophrenic patients. Thus, there is no evidence for reproductive compensation by relatives. Furthermore, decreased fertility has also been described in other psychiatric diseases (Slater et al. 1971; Vogel 1979).

The concept of a balanced polymorphism in schizophrenia rests on a superficial analogy with Mendelian traits, whereas the clinical phenotype that is summarized as "schizophrenia" presumably has a highly heterogenous etiology, both from the genetic (Vogel and Propping 1982) and exogenous influences. Under these conditions there is no basis to expect any compensation for the reproductive deficit of schizophrenics.

4. Conclusions

There is almost complete agreement in the literature that the marriage rate of schizophrenics is reduced. The rates range from 30% to 40% for males and 50% to 60% for females compared to the general population, the sex difference being mainly due to the later onset of the psychosis in females. With respect to marital fertility, the data are not consistent. Most authors agree that during marriage fertility is slightly reduced, lying between 70% and 80% of the expected values. The total rate of reproduction of schizophrenics is markedly reduced, the value being 30% to 80% of the population average. This decrease is mainly due to a reduced probability of marriage. It has to be remembered that differences in marriage and fertility rates between different investigations are at least partly due to selection effects such as socioeconomic level, race, institutionalization, time of assessment, chronicity of the illness (Lane 1971).

We did not refer to the incidence of illegitimate births in schizophrenics. Although their rate is increased above population average, those authors who examined the problem agree that illegitimate births can by no means compensate for the reproductive deficit of schizophrenics.

It had earlier been hypothesized that healthy relatives of schizophrenics would have a higher fertility than the general population and thus would compensate for the reproductive deficit of the schizophrenics. There is, however, almost no empirical evidence for such an assumption.

One study reported an increase of marriage rate and total rate of reproduction of schizophrenics admitted to the hospital between the fourth and sixth decade of this century, as compared with the general population. Other investigations which also claim to show a reduction of the reproductive deficit of schizophrenics suffer from methodological shortcomings. Therefore, the relative increase of fertility in schizophrenics remains so far an unconfirmed finding.

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