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Genetic Hypotheses and Environmental Factors in the Light of Psychiatric Morbidity in the Families of Schizophrenics

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Summary. The hypothesis that schizophrenia and some non-psychotic abnormalities occurring in the close relatives are both manifestations of a unitary 'schizoid state' due to a major dominant gene is further examined. Comparisons are made (1) of the observed and expected frequencies of the different types of parent mating; and (2) of the observed and expected risks among sibs in families with neither, or with one or both, of the parents abnormal. It is concluded that the results do not fit well with the model of inheritance of the schizoid state through a major dominant gene.

Since some hereditary contribution in schizophrenia can be regarded as established, the excess of personality disorders and heavy drinking in the families is thought to be due to a combination of polygenic inheritance and environmental influences. The findings are regarded only as tentative, but suggest several hypotheses which could be tested.

Introduction

In a previous paper (Stephens *et al.*, 1975) the results of a study of the psychiatric morbidity in the parents and sibs of schizophrenic and non-schizophrenic patients were described. One of the aims of the study was to test the theory of dominant inheritance of 'schizoid disease' proposed by Heston (1970). Heston claimed that while only a small fraction of heterozygotes ever manifested the actual psychosis, most of the remainder showed clinical disabilities, often denoted as 'schizoid', and that if these were taken into account the theoretical mendelian ratio of 50 per cent first-degree relatives affected was observed. This constituted a natural extension of the theory (Slater, 1958; Slater and Cowie, 1971) that schizophrenia is inherited through a partially dominant (or intermediate) gene which manifests as the psychosis in all homozygotes and in a proportion only of heterozygotes.

In our sample (Stephens *et al.*, 1975), mental subnormality, suicide, functional psychoses other than schizophrenia, and personality disorders of neurotic type were all fairly evenly distributed between the schizophrenics' families and the controls, while neurotic reactions were significantly commoner in the latter. Apart from schizophrenia itself, only non-neurotic (i.e. paranoid, schizoid or psychopathic) personality disorders and heavy drinking were significantly more common in the schizophrenics' families; and these conditions appeared, therefore, to have the strongest claim to be regarded as manifestations of the heterozygous state. However, it was found that the observed risks did not fit well with the model of dominant inheritance proposed by Heston.

In this paper, the findings in the schizophrenics' families are examined further, bearing in mind the predictions which follow from the major gene hypothesis about the frequency of

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types of parental mating, and the risks of abnormality in the sibs, when neither parent, or one parent, is affected.

Method

The method of collecting the sample and the definitions used have been fully described (Stephens *et al.*, 1975). The results reported here are based on the 57 families of schizophrenics in which information about the psychiatric state of both parents was available, and on 50 of these families in which at least one sib had reached the age of 18.

Results

The type of parental mating

If schizophrenia is inherited through a major, partially dominant, gene, then, except in the unlikely event of mutation, at least one of the parents must possess the gene. Assuming that all, or nearly all, of the heterozygote carriers can be clinically identified, there would, except in the case of illegitimacy, be few families, or none, in which neither parent was affected. Furthermore, one would expect to find that abnormal parents tended to be married to normal partners, and that, unless the frequency of the gene was much higher than the 3 per cent proposed for the schizophrenia gene by Slater and Cowie (1971), or unless there was a considerable degree of assortative mating, marriages where both patients were abnormal would be rare.

If in our sample we counted as possible heterozygotes only those parents with schizophrenia (one) and personality disorders diagnosed as paranoid or schizoid (21 parents), nearly all the affected parents would be mothers. To obtain fathers, we need to count, in addition, psychopathic personalities and also those heavy drinkers in whom another abnormality of non-neurotic kind was also diagnosed or strongly suspected (Definition 1). There are then 19 mothers and 12 fathers belonging to 26 families. Both parents are affected in 5 (9 per cent) and neither parent in 31 (53 per cent) of the 57 families.

If the criteria are further extended to include all types of personality disorder and all heavy drinkers (Definition 2), there are 23 mothers and 23 fathers belonging to 35 families. Both parents are affected in 11 (19 per cent) and unaffected in 22 (39 per cent). Finally, if the remaining 4 psychotic (non-schizophrenic) and 5 neurotic parents are included (Definition 3), both parents are affected in 15 (26 per cent) of the families and neither parent in 17 (30 per cent). Table I shows how the types of parental marriages are distributed when these different criteria of abnormality are applied. The distributions observed are obviously quite different from expectation, since there are always far too many families with neither parent affected.

By arbitrarily varying the rate of manifestation of the gene, we can readily obtain expectancies for marriages with two normal parents which are similar to those observed. (The method of calculation is shown in the Appendix.) However, the proportions of families expected to have both parents affected are then much lower than those observed (Table I),

Table I

Type of parental marriage (N = normal parent; A = affected parent) using different criteria of abnormality (see text)

Parents	Definition 1			Definition 2			Definition 3		
	Observed nos.	Expected nos. with Dominance and 40% manifestation	Expected nos. with Random pairing	Observed nos.	Expected nos. with Dominance and 60% manifestation	Expected nos. with Random pairing	Observed nos.	Expected nos. with Dominance and 70% manifestation	Expected nos. with Random pairing
N×N	31	31·4	30·0	22	20·3	20·3	17	15·0	15·1
N×A	21	24·3	23·0	24	33·9	27·4	25	38·2	28·8
A×A	5	1·3	4·0	11	2·8	9·3	15	3·8	13·1

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and the data clearly do not fit the model of dominant inheritance. On the other hand, the distributions agree quite well with what one would expect to find in the absence of a major gene.

The parental marriage and the risks of abnormality in the sibs

With dominant inheritance, the risk of abnormality in the sibs of probands in families where one parent is affected (N×A) is usually not much higher than the risk when neither parent is affected (N×N). If, for example, we assume a population frequency for the trait caused by the presence of the schizophrenic gene (i.e. schizophrenia plus its 'spectrum') of 3·5 per cent and a high rate of manifestation of 60 per cent, then about 30 per cent of sibs would be affected irrespective of the state of the parents (Vogel and Krüger, 1967). On the other hand, an increase in the risk by a factor of 2·5 or more, when one parent is affected, would strongly favour a polygenic model. For high population frequencies, however, the increase would be smaller, and the test would be less discriminating.

To make a comparison with the data, the families with one or both parents affected (N×A, A×A) are combined, since, as already shown, the number with both affected is incompatible with dominant inheritance, and we have to suppose that in most of these families only one of the parents possessed the gene.

With Definition 1, about 14 per cent of the sibs are affected (applying the same criteria as for the parents), irrespective of the state of the parents. With Definitions 2 and 3 the risks are somewhat increased in the N×A and A×A families. Table II shows the results using Definition 2, which gives the largest difference. The risk among the sibs increases from 16 per cent to 26 per cent, which is not significant and would be compatible with dominance.

There is, however, a difference between brothers and sisters, which is also shown in Table II. The sisters were not affected at all by the condition of their parents. In the case of brothers, the risk increased significantly ($p < \cdot 01$) from 15 per cent to 43 per cent, which fits well with a polygenic model, in which the theoretical risk with neither parent affected would be in the region of 15 per cent, and with one parent affected about 40 per cent (Vogel and Krüger, 1967).

The increased risk in the brothers is partly, but not wholly, due to one exceptional family with three schizophrenic sibs, in addition to the proband. There is also in the N×A and A×A families a high proportion of brothers with psychopathic disorders, conditions which are thought to have strong social determinants. This aspect is taken up in the next section.

Abnormality in the fathers and sibs and the effects of social class

The relationship between the type of parental

TABLE II

Type of parental marriage and risk of abnormality in sibs of schizophrenics

	N×N			N×A, A×A		
Number of families	20			30		
Number of sibs	Brothers 33	Sisters 31	Sibs 64	Brothers 49	Sisters 48	Sibs 97
Schizophrenia	1	0	1 } (16%)	7	3	10 } (26%)
Personality disorder/heavy drinking	3	6	9 }	13	2	15 }
Other abnormality	1	2	3 (4%)	1	4	5 (5%)
Total abnormal (%)	5(15%)	8(26%)	13(20%)	21(43%)	9(19%)	30(31%)

A = Schizophrenia, any type of personality disorder, or heavy drinker.
N = Normal or any disorder not included in A.

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mating and the risk of abnormality in the sibs has just been described. With one or both parents affected the brothers, but not the sisters, of schizophrenics were more likely to be abnormal than when both parents were unaffected. When the fathers and mothers are considered separately, however, a surprising difference becomes apparent; the abnormal brothers are concentrated in the families with abnormal fathers, and the mothers' state has no effect on the condition of the brothers (Table III).

These findings, if confirmed, might be given an environmentalist interpretation. Fathers of schizophrenics often show aberrations of behaviour associated with violence, heavy drinking or criminality, and are more likely to be the cause of psychopathic reactions in their offspring than the mothers, whose abnormalities are usually of a less overtly disturbing and disruptive nature. Male offspring may be more susceptible to their father's aberrations and more likely to react to them with behavioural disturbances than female offspring. This explanation would accord with the importance usually attached to environmental factors in the aetiologies of psychopathy and heavy drinking in general.

In keeping with this view, nealy all the sibs with psychopathic disorder and/or heavy drinking belong to families in which the fathers were of social classes IV or V (Stephens *et al.*, 1975). However, when the psychiatric state of the father was taken into account, it was found that the family's social class had little or no effect when the father was normal, but increased the risk of psychopathy or alcoholism significantly when the father was abnormal (Table IV). The risk in male sibs with an abnormal father of social classes IV or V was 65 per cent. This may simply have been a direct consequence of the father's overt behaviour, but if heredity is an aetiological factor in psychopathic disorders, as recent evidence indicates (Schulsinger, 1972), we may be seeing the effects of genetic-environmental interaction.

Abnormalities in the mothers and the sex and marital state of the probands

Alanen (1968) reported that psychopathology in the fathers of schizophrenics was as severe and as frequent as in the mothers. We succeeded in interviewing only a small proportion of the fathers, but our general findings are in agreement with Alanen's, provided that persistent heavy drinking is regarded as a sign of psychopathology. We noted, however, that the mothers of male schizophrenics were significantly more often abnormal in some way than the mothers of female schizophrenics (Table V), while the fathers and sibs did not show this difference. This pattern is not easy to account for on a purely genetic basis, and seems to require some

TABLE III

Effect of abnormality in mothers compared with abnormality in fathers on sibs of schizophrenics

	Mothers			Fathers		
	Normal	Abnormal		Normal	Abnormal	
Number of families*	25	25		28	22	
Number of sibs at risk	91	70		90	71	
Sibs with			p			p
Schizophrenia	6	5	n.s.	2	9	<·01
Personality disorder/heavy drinking	16	8	n.s.	9	15	<·05
Other abnormality	5	3		3	5	
Total abnormal sibs	27	16		14	29	
Total normal sibs	64	54		76	42	<·01
Sibs interviewed	37%	24%		27%	38%	

* i.e. Families containing at least one sib.

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TABLE IV

Mental state and social class of fathers and abnormalities in sibs of schizophrenics

	Fathers' mental state*				
	Normal		Abnormal		Total
	S.C. I–III	S.C. IV–V	S.C. I–III	S.C. IV–V	
Sibs with:					
Schizophrenia ..	0 } 5%	2 } 8%	2 } 8%	6 } 38%	10
Psychopathic personality/ heavy drinking ..	1	3	0	9	13
Other abnormalities..	2	5	6	4	17
Total abnormal ..	3 (15%)	10 (17%)	8 (32%)	19 (45%)	40
Total normal ..	17 (85%)	50 (83%)	17 (68%)	23 (55%)	107
Number of sibs ..	20(100%)	60(100%)	25(100%)	42(100%)	147

* Excluding 4 families where Social Class of father is unknown.

TABLE V

Abnormalities in mothers of schizophrenics by sex of proband

Mothers	Male probands	Female probands	p
Schizophrenia ..	1	0	
Personality disorder/ heavy drinking	15	5	
Other psychosis	2	1	
Neurotic disorders	7	2	
Total abnormal	25 (66%)	8 (35%)	<·05
Normal ..	13 (34%)	15 (65%)	
All mothers ..	38(100%)	23(100%)	
Interviewed ..	30	18	
Dead ..	8	4	
Refused ..	0	1	

other explanation. It is possible, for example, that mothers are particularly prone to become anxious or disturbed as a result of the illness of their sons.

In some families it was obvious that the mothers were extremely involved emotionally with their schizophrenic offspring. Some of them denied that the patient was ill, opposed treatment, or even appeared to share some of the patient's delusions. However, it seems probable that in these near-psychotic borderline states exposure to the illness had at most made overt an existing abnormality or predisposition.

In other families we had the impression that the mother's state was a quite understandable reaction to her experiences in connection with the patient's illness and often repeated admission to hospital. In either case, we would expect to find a relationship between disorders in the mothers of schizophrenics and the duration or intensity of their exposure to the psychosis. We have no direct observations on this point; but it was noted that female schizophrenics who were married had the least disturbed mothers (one abnormal out of eight), and that the risk in these mothers was significantly lower than in the mothers of the other patients (Table VI). It seems that the marriages of the schizophrenic daughters, though apparently not of the sons, had tended to shield the mothers from the effects of the illness. Whatever the explanation, the differential risk in mothers

TABLE VI

Abnormalities in mothers according to marital state of probands

Mothers	Male probands		Female probands	
	Single	Married	Single	Married
Normal ..	10	3	7	8
Abnormal ..	20	5	7	1
Total ..	30	8	14	9

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of male and female patients is evidently largely due to the good health possessed by the mothers of the married females.

Discussion

In a previous paper (Stephens *et al.*, 1975) the types of psychiatric morbidity found in the parents and sibs of schizophrenic patients were reported and contrasted with those in the relatives of a sample of non-schizophrenic patients. It was concluded that 'non-neurotic personality disorders' (i.e. paranoid, schizoid or psychopathic personality) and some cases of heavy drinking in which a personality disorder was suspected were the conditions most likely to be biologically akin to schizophrenia, at least in such families. In the present paper the occurrence of these and other psychiatric abnormalities in the parents and sibs of the schizophrenics has been examined in greater detail and compared with expectations based on genetic models.

The approach was entirely clinical, and psychiatric diagnosis, specially in the area of personality, is known to be unreliable; but no objective psychological or physiological measure of 'schizoidness' is available. Only one-third of the relatives were seen personally, and since personality disorders and neurotic reactions (though not heavy drinking or other disorders) were much more frequently diagnosed among interviewed than among non-interviewed relatives (Stephens *et al.*, 1975) the risks of these abnormalities will have been under-estimated. However, careful examination of the proportions of relatives interviewed in the various subgroups does not suggest that the differences found can be explained away by unevenness in interviewing rates. Nevertheless, it is recognized that any conclusions drawn from the data must be regarded as extremely tentative. Our aim in the following discussion is to put forward certain interpretations for future testing, and in the hope of stimulating interest in the nature of non-psychotic abnormalities occurring in schizophrenics and their families.

Personality disorders in schizophrenics and their relatives

The comparative scarcity of paranoid or schizoid disorders of personality in the relatives, other than the mothers, deserves comment. Only four such diagnoses were made among the 73 interviewed fathers and sibs. It is quite probable that in some individuals attention was distracted from the schizoid abnormality by their psychopathic behaviour or drinking habits. Others who were shy or withdrawn may not have been recognized as abnormal because they did not wish to be interviewed and their relatives did not think of them as unusual. More fundamental, however, are the reports showing that only a minority of schizophrenics themselves are markedly schizoid before the onset of the illness (Bleuler, 1972; Gottesman and Shields, 1972).

Now Gottesman and Shields (1972) noticed that their MZ twins were quite similar in personality when this was categorized as schizoid, otherwise abnormal or normal, indicating that personality is to some extent under genetic control. It would follow that schizoid traits might be expected in the close relatives of those schizophrenics whose personalities were schizoid, but that other traits might be found when the personality of the schizophrenic was, for example, psychopathic, obsessional or cyclothymic. All these traits were met with in greater or less degree both in our schizophrenic patients and in their relatives, though a systematic study has not been possible. However, it would appear to be futile to attempt to establish a risk of 'schizoidness' which was true for the members of the families of *all* schizophrenics. Moreover, whatever the nature of the underlying trait, its clinical manifestation appears likely to be influenced by the individual's sex and by environmental factors such as social class. The findings in this study reinforce the observations of other workers to suggest that the premorbid personality of schizophrenics, and the relationships of the different forms of personality deviation found in the first degree relatives to the illness of schizophrenic probands and to incidental factors, require reinvestigation with the aid of modern methods.

Mode of inheritance

According to the theory that schizophrenia is inherited through a major partially dominant gene with 25 per cent or less manifestation in

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heterozygotes (Slater and Cowie, 1971) there would be four or more non-psychotic carriers for every person with schizophrenia. By assuming that most, if not all, forms of conspicuous psychiatric morbidity occurring in the close relatives of schizophrenics are manifestations of a schizoid state due to this gene, it has been possible to advance an impressive case in favour of the monogenic theory of schizophrenia, (Heston, 1970).

However, the results described in the previous paper (Stephens *et al.*, 1975) indicate that, while schizophrenic families are characterized by an excess of personality disorders of non-neurotic kind and habitual heavy drinking, other forms of morbidity are not particularly frequent, and are unlikely, therefore, to have any relationship to schizophrenia.

This finding, and the pattern of occurrence of schizophrenia and personality disorders in the families of our schizophrenics described in this paper, provide little support for the hypothesis of a unitary schizoid disorder inherited through a single dominant gene. This must to some extent weaken the monogenic theory of schizophrenia, although Slater's (1958) theory makes no assumptions as to the condition of the unaffected heterozygotes. However, some contribution from heredity in schizophrenia can be regarded as established, and there is evidence from adoption studies (Rosenthal *et al.*, 1968) of a biological relationship between schizophrenia and certain types of personality disorder. We seem, therefore, to be left with a polygenic hypothesis, in which the type of abnormality manifesting in predisposed persons is strongly influenced by the environment, by sex and probably also by other constitutional factors. It has to be admitted, however, that uncertainties about population frequencies, aetiological heterogeneity and clinical diagnosis make the tests proposed for discriminating between monogenic and polygenic inheritance particularly difficult to apply in the case of 'spectrum disorders' which include deviations of personality not sharply differentiated from the norm.

Environmental factors

Hereditary and environmental factors prove difficult to disentangle. The abnormalities observed in the mothers of schizophrenic probands are a case in point. They may have been vividly depicted in the accounts of a number of investigators (Alanen, 1966; Lidz *et al.*, 1965). In some cases, and this applied to the families we investigated, their patterns of thought and behaviour, and their acceptance of some of the patient's delusional beliefs, suggested a near-psychotic state. Of all the abnormalities met with, these seem most likely to be genetically related to schizophrenia. Even so, it should not be assumed that environmental factors play no part in aetiology.

There is, in fact, evidence that psychosis can be induced *in predisposed individuals* through exposure to the schizophrenic illness of another person (Abe, 1969; Scharfetter, 1972). Our findings suggest that, in the case of the mothers of schizophrenics, abnormalities other than overt psychosis may also be induced or aggravated by exposure to the schizophrenic illnesses of their sons.

No plausible genetical explanation for the association between schizophrenia in the sons and conspicuous abnormality in the mothers can be advanced. Now, if the association had arisen from the schizophrenogenic effects of the mothers' personality aberration one would have expected a significant excess of abnormal sibs in the families in question. But manifest psychopathology among the sibs was much more impressively linked with deviation in the fathers. It is very tempting to link the much lower prevalence of abnormality among the mothers of schizophrenic daughters than sons with the higher rate of marriage observed among the former, which would be associated, presumably, with a lower prevalence of premorbid personality aberrations among them. Both these factors would make for shorter periods of exposure to the influence of psychotic or deviant individuals, and the onerous stress of caring for them. A possible example of interaction between members of the family which could give rise to detrimental effects on personality development is provided by the concentration of abnormal brothers (but not sisters) in the families in which the fathers were judged to be abnormal. These fathers often exhibited marked anomalies of personality, such as psychopathy or heavy

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drinking. The evidence suggested that this phenomenon was also unlikely to reflect genetical transmission of a *forme fruste* of schizophrenia. Behind the association with social class lurked the much higher prevalence of abnormal fathers in social classes IV and V. If hereditary-environmental interaction was at work then the relevant genetical factors seem at least as likely to have been concerned with psychopathy as with schizophrenia.

The concentration of abnormal sibs in the families of abnormal fathers highlights the general point that members of families in which some genetically determined form of disabling disease is prevalent are more liable than the general population to become espoused to individuals who are themselves abnormal in one or more ways. They, therefore, exert an adverse influence on the environment in which their offspring are reared in their formative years as well as on their chances of acquiring a normal endowment of genes. It is well known that a conglomeration of disabilities accumulates in this manner in the families of those with Huntington's chorea (Hans and Gilmore, 1968; Dewhurst, Oliver and McKnight, 1970).

For the reasons indicated the situation in relation to schizophrenia is likely to be more complex. However, the findings recorded here raise important questions about the personality characteristics of the fathers of those born to schizophrenic mothers and reared from an early age in orphanages or by foster parents. The observations are particularly germane in view of the fact that most of the psychiatric morbidity placed on record (Heston, 1966; Rosenthal *et al.*, 1968) has been in the form of 'borderline' states, 'schizoid' personality, or various kinds of neuroses or psychopathy.

In conclusion, the psychiatric disorders to be found among the first degree relatives of schizophrenic probands do indeed range over a broad spectrum. But these conditions are not all necessarily related genetically to schizophrenia. Assortative mating determined by psychological or social factors and environmental causes may contribute to a significant extent in their causation. And it cannot be assumed that the relevant genetical and other causes of such 'spectrum disorders' are identical with those underlying the cases of indubitable schizophrenia found in the same family.

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References

Abe, K. (1969) The morbidity rate and environmental influence in monozygotic co-twins of schizophrenics. *British Journal of Psychiatry*, **115**, 519–31.

Alanen, Y. O. (1966) The family in the pathogenesis of schizophrenic and neurotic disorders. *Acta Psychiatrica Scandinavica*, Supplement 189.

—— (1968) From the mothers of schizophrenic patients to interactional family dynamics. In *The Transmission of Schizophrenia* (eds. Rosenthal and Kety), pp. 201–12. Oxford: Pergamon Press.

Bleuler, M. (1972) *Die Schizophrenen Geistesstörungen im Lichte langjähriger Kranken- und Familiengeschichten.* Stuttgart: Thieme.

Dewhurst, K., Oliver, J. E. & McKnight, A. L. (1970) Socio-psychiatric consequences of Huntington's disease. *British Journal of Psychiatry*, **116**, 255–8.

Gottesman, I. I. & Shields, J. (1972) *Schizophrenia and Genetics.* New York and London: Academic Press.

Hans, M. B. & Gilmore, T. H. (1968) Social aspects of Huntington's Chorea. *British Journal of Psychiatry*, **114**, 93–8.

Heston, L. L. (1966) Psychiatric disorders in foster home reared children of schizophrenic mothers. *British Journal of Psychiatry*, **112**, 819–25.

—— (1970) The genetics of schizophrenia and schizoid disease. *Science*, **167**, 249–56.

Lidz, T., Fleck, S. & Cornelison, A. (1965) *Schizophrenia and the Family.* New York: International Universities Press.

Rosenthal, D., Wender, P. H., Kety, S. S., Schulsinger, F., Welner, J. & Østergaard, L. (1968) In *The Transmission of Schizophrenia* (eds. Rosenthal and Kety). Oxford: Pergamon Press.

Scharfetter, C. (1972) Studies of heredity in symbiotic psychoses. *International Journal of Mental Health*, **1**, 116–23.

https://doi.org/10.1192/bjp.127.2.109 Published online by Cambridge University Press

SCHULSINGER, F. (1972) Psychopathy: heredity and environment. *International Journal of Mental Health*, 1, 190–206.

SLATER, E. (1958) The monogenic theory of schizophrenia. *Acta Genetica et Statistica Medica (Basel)*, 8, 50–6.

—— & COWIE, V. (1971) *The Genetics of Mental Disorders*. London and New York: Oxford University Press.

STEPHENS, D. A., ATKINSON, M. W., KAY, D. W. K., ROTH, M. & GARSIDE, R. F. (1975) Psychiatric morbidity in the parents and sibs of schizophrenics and non-schizophrenics. *British Journal of Psychiatry*, 127, 97–108.

VOGEL, F. & KRÜGER, J. (1967) Multifactorial determination of genetic affections. *Proceedings 3rd International Congress Human Genetics*, Chicago, 1966.

APPENDIX

Method of calculating percentages of families of schizophrenics having neither, one or both parents affected

Adapted from Slater and Cowie (1971), p. 61

Parental mating	(1) Frequency of mating in whole population	(2) Weights	(3) Frequency of mating in families of schizophrenics	(4) Weights for affected parents		
				Both	One	Neither
AA × Aa	$4p^3(1-p)$	$\frac{1}{2}(1+m)$	$2(1+m)p^3(1-p)$	M	$1-M$	0
AA × aa	$2p^2(1-p)^2$	m	$2mp^2(1-p)^2$	0	1	0
Aa × Aa	$4p^2(1-p)^2$	$\frac{1+2m}{4}$	$p^2(1-p)^2(1+2m)$	M^2	$2(1-M)M$	$(1-M)^2$
Aa × aa	$4p\,(1-p)^3$	$\frac{1}{2}m$	$2mp(1-p)^3$	0	M	$1-M$

Where p = frequency of schizophrenia gene;
m = rate of manifestation of schizophrenia in heterozygotes;
M = rate of manifestation of 'schizoid state' in heterozygote parents.

Example 1

If p = ·03, m = ·13, and M = 1, then:

Parental mating	(3) Frequency of mating in families of schizophrenics	(4) Weights for affected parents			Columns (3) × (4)		
		Both	One	Neither	Both	One	Neither
AA × Aa	·000 057	1	0	0	·000 057	0	0
AA × aa	·000 220	0	1	0	0	·000 220	0
Aa × Aa	·001 068	1	0	0	·001 068	0	0
Aa × aa	·007 119	0	1	0	0	·007 119	0
	·008 464				·001 125	·007 339	0

Percentages of families with:

Both parents affected = $\frac{\cdot 001\ 125}{\cdot 008\ 464} \times 100 = 13 \cdot 3\%$

One parent affected = $\frac{\cdot 007\ 339}{\cdot 008\ 464} \times 100 = 86 \cdot 7\%$

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Example 2

If M = 0·60, then:

Parental mating	(3) Frequency of mating in families of schizophrenics	(4) Weights for affected parents			Columns (3) × (4)		
		Both	One	Neither	Both	One	Neither
AA × Aa	·000 057	0·60	0·40	0	·000 034	·000 023	0
AA × aa	·000 220	0	1	1	0	·000 220	0
Aa × Aa	·001 068	0·36	0·48	0·16	·000 384	·000 513	·000 171
Aa × aa	·007 119	0	0·60	0·40	0	·004 271	·002 848
	·008 464				·000 418	·005 027	·003 019

Percentage of families with:

Both parents affected = $\frac{\cdot 000\ 418}{\cdot 008\ 464} \times 100 = 4{\cdot}9\%$

One parent affected = $\frac{\cdot 005\ 027}{\cdot 008\ 464} \times 100 = 59{\cdot}4\%$

Neither parent affected = $\frac{\cdot 003\ 019}{\cdot 008\ 464} \times 100 = 35{\cdot}7\%$

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