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SOME FACTORS ASSOCIATED WITH CONCORDANCE AND DISCORDANCE WITH RESPECT TO SCHIZOPHRENIA IN MONOZYGOTIC TWINS

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One of the interesting issues raised by geneticists regarding schizophrenia is referred to as "the biological unity of schizophrenia" and "the specificity of the schizophrenic genotype." Planansky (14) has provided a brief review of the literature concerned with this problem. In the main, relevant research has involved attempts to establish any one or more of four points: 1) differentiation of the manic-depressive from the schizophrenic genotype; 2) identification of a non-hereditary subgroup within the domain of schizophrenia; 3) genetic differentiation of the main Kraepelinian subtypes; 4) genetic differentiation of typical, or "process," from atypical or "reactive" schizophrenia. Following Planansky, we may summarize this literature briefly as follows.

1. *Specificity of the manic-depressive and schizophrenic genotypes.*
   a. Rüdin (17) noted that manic-depressive psychosis rarely occurred in the children of schizophrenic subjects, but occurred rather often among these subjects' parents. Since he adhered to a strict specificity theory, he tried to explain this puzzling finding by postulating a complex Mendelian segregation and interrelation between the two illnesses.
   b. Schulz (18) found large numbers of schizophrenics among the children of two parents with affective psychosis, whereas among the children of two schizophrenic parents, manic-depressive psychoses were very rare. Both psychoses were thought to occur more frequently in the same families than would be expected by chance alone, and he thought that there might be a genetic relationship between the two psychoses.
   c. Penrose (12) used extensive data from the Ontario mental hospitals and found that the same family often included both types of illness.
   d. Kallmann (7) believed that confusion resulted from faulty diagnosis. He stated that when diagnostic criteria were sharply defined as in his study, there was not one dizygotic twin pair with a schizophrenic psychosis in one member and a manic-depressive psychosis in the other, nor a single manic-depressive index family with an authentic case of schizophrenia among the parents and siblings of the index cases. Unfortunately, he does not present figures regarding the reliability of diagnostic differentiation when his criteria are used.
   e. Planansky (14) pointed out that there has not been one clear-cut case of monozygotic twins where one twin was schizophrenic and the other manic-depressive. This statement must be taken with reservation, since affective psychosis in one twin is not rare when the other twin is schizophrenic. Problems of diag-

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nostic reliability are even more clearly at issue in such matters.

2. *Identification of a non-hereditary subgroup.*
   a. Such a subgroup was thought to be found by Bleuler (3). He thought of it as a separate disease within the group of schizophrenias. Planansky however thought that, statistically, the distinction did not appear to be substantiated in Bleuler's sample.
   b. Rosanoff, Handy, Plesset and Brush (16) also thought that they had evidence that hereditary factors were not necessarily involved in schizophrenia, since they believed that the frequency of schizophrenia was higher among their dizygotic cotwins than among siblings of schizophrenic index cases. Kallmann (7) found no such difference.
3. *Genetic differentiation of the Kraepelinian subtypes.*
   a. Kallmann (6) found a higher rate of schizophrenia among the children of hebephrenic and catatonic patients than among the children of simple and paranoid schizophrenics. The rates were 20.7, 21.6, 10.4 and 11.6 per cent for the children of hebephrenic, catatonic, simple and paranoid schizophrenics respectively. Analyzing the data by Schulz's method, he concluded that the findings were compatible with an hypothesis of biological homogeneity. Slater (19), however, analyzed the data differently and concluded that the clinical subtypes were genetically heterogeneous.
   b. Zehnder (21) compared schizophrenic siblings regarding their subtype diagnosis. She found equal proportions of sibships with similar or with dissimilar forms, and concluded in favor of biological homogeneity of schizophrenia. Otherwise, she questioned, why should dissimilar forms occur in sibships at all? Slater (19), however, reanalyzed Zehnder's data, found that the distribution of Kraepelinian subtypes in pairs of siblings showed a strong positive correlation, and attributed this similarity to the action of common modifying genes.
   c. Elsässer (4) found that the schizophrenic children of two schizophrenic parents with the same subtype diagnosis did not always belong to the same subtype as their parents. This led him to conclude that the Kraepelinian forms were genetically interchangeable.
4. *Genetic differentiation of typical from atypical schizophrenia.*
   a. Leonhard (8) found that his typical cases with deteriorative outcome showed much *less* apparent heredity than atypical cases which had a more variable course of illness and favorable prognosis.
   b. Elsässer (4) found that when both parents were schizophrenic, if the child had a psychosis at all it was likely to be schizophrenic. However, this was true primarily if the parents had a "typical" form of schizophrenia, suggesting that this type had a more direct hereditary effect with respect to schizophrenia than nontypical forms.

From this brief summary it can be seen that although the issues are of fundamental importance we are not in a position to draw conclusions with confidence about any one of them. Planansky concluded that twin studies were more promising as a method of attacking these problems than analyses of sibships and other family groupings.

In this study a novel method of analysis of a sample of twins has been used to approach the question of biological unity in schizophrenia.[2] The method involves only

[2] The rationale for this method has been stated most aptly by Allen (1) as follows. "It is likely that for many medical conditions the same clinical picture may be produced either by heredity or by

monozygotic twins. The twin pairs in the sample who are concordant with respect to the criterion, in this case schizophrenia, are compared with the pairs who are discordant. The comparisons made are dictated by specific hypotheses proposed by the investigator.

It was reasoned as follows. If there is a significant genetic factor in schizophrenia, it is especially likely to be represented among the one-egg twin pairs if both twins have the illness. Conversely, if there is a subgroup of schizophrenia which has either no hereditary basis or one which is only mildly contributory, this subgroup should be more likely to be represented in a group of one-egg twins in which only one twin has the illness.

Specifically, the hypotheses proposed were as follows.

1. Typical or process schizophrenia is found more frequently among concordant pairs, atypical or reactive schizophrenia occurring more often among discordant pairs of one-egg twins.

2. The severity of the illness is greater in concordant than in discordant twins.

3. History of schizophrenic illness is found more frequently in the families of concordant than of discordant twin pairs.

METHOD

Obtaining a well-selected sample of identical twins with at least one of the pair schizophrenic involves a tremendous output of time and effort. Such samples are therefore rare—there are in existence only five twin studies which have paid attention, however adequate, to problems of sampling: Luxenburger (9), Rosanoff *et al.* (16), Essen-Möller (5), Kallmann (7) and Slater (20). The yield of subjects in such studies is so small that it behooves us to extract as much information as we can from them.

Lacking the original data, one can make the proposed type of analysis only if the case histories are fairly detailed and if all, or almost all, the cases are published. Only the Essen-Möller (5) and Slater (20) studies meet these criteria. Unfortunately, in the Essen-Möller study there are only seven pairs of identical twins of whom at least one was said to be clearly schizophrenic, and these are too few for separate analysis. In the Slater sample there are 37 such monozygotic twin pairs, and their case histories are published in sufficient detail to make tests of the above hypotheses possible.

Slater's case histories provide the raw data for the present study.[3] Methodologically, there is a great advantage in testing the above hypotheses with data collected and published by another investigator who did not have these hypotheses in mind at the time of the original investigation. This virtually insures against the intrusion of bias which could unwittingly slant the collection or reporting of data either for or against these hypotheses. Unfortunately, such analyses are only occasionally possible, since the relevant data usually have not been obtained or published in the original report.

The cases were not simply dichotomized as process or reactive. Rather, a method was used which yielded a range of scores on a continuum related in most important respects to this dichotomy. Ratings were made from the histories of each twin's premorbid social and sexual adjustment, using the Phillips Scale of Premorbid Adjustment

environment. In such a case, a sample of single-born probands will contain a proportion of the environmental cases, or phenocopies, and a family study has to start out by lumping the relatives of both types of case. If, however, one starts with monozygotic twins as probands, a separation of the concordant and discordant pairs will in general segregate the genetic cases from the phenocopies. This permits from the outset a separate analysis of two groups of relatives practically without reference to familial incidence, so that the latter can be studied as an independent variable in the cases presumed to be genetic. Even with a very incomplete separation of genetic from non-genetic cases, the method may bring to light important statistical differences between the two groups of relatives. At the least, this method of analysis provides another type of internal control in twin studies."

[3] The author acknowledges gratefully Dr. Slater's spirit of scientific co-operation in making his case material available to interested investigators for study and evaluation.

TABLE 1
Phillips Premorbidity Scores of the Monozygotic Male Twins*

Concordant pairs			Discordant pairs		
Case #	Index case	Cotwin	Case #	Index case	Co-twin
30†	25	25	61†	22	22
80/174	27‡	24‡	133	20	9
87	24	21	202	24	16
240	25	28	231	22	15
287	20	23	17	21	15
			160†	19	19
Sum	121	121	Sum	128	96
$\bar{X}$	24.2	24.2	$\bar{X}$	21.3	16.0
S.D.	2.32		S.D.	1.60	4.00

* Phillips divided his scale so that subjects scoring 15 and above were called premorbid poors, 14 and below premorbid goods. Garmezy has felt that the middle range of scores, around 15, are less reliable prognosticators than more extreme scores.

† In Cases 30, 61, and 160, not enough information is provided to permit differentiation of the twins by these ratings.

‡ Since both twins are index cases, a coin was tossed to decide which twin to place in which column. This is done merely for presentational purposes and affects none of the conclusions.

(13). The scale yields a range of possible scores from 2 to 30; the higher the score, the poorer the patient's adjustment prior to his illness. At the lower end of the range of scores, subjects are called "premorbid goods," and at the higher end, "premorbid poors." The "goods" have a favorable prognosis, the "poors" unfavorable. In respect to prognosis as well as social and sexual history, the "poors" are representative of the group usually referred to as process, typical, nuclear, etc., while the "goods" are representative of patients ordinarly called reactive, atypical, peripheral, psychogenic, etc. Since the Phillips Scale has been validated for male subjects only, the rating could be made only for the male twins. The scale has been used with considerable success at Duke University in its program of research on the psychology of schizophrenia (15).

Reliability of the Phillips premorbidity ratings is found to be good even when social and sexual histories are only fragmentary. In order to check upon this a separate sample of case histories was obtained, about as detailed as Slater's. These were rated independently by two judges and the writer. One judge made Phillips premorbidity ratings on seven cases, and the other, a more sophisticated judge, made ratings on five cases. The average difference between the judges' ratings and mine was 2.7 and 2.0 scale points respectively.

As indices of the severity of illness, the patient's age at the time he was first admitted as schizophrenic to a clinic or hospital was used, as well as Slater's evaluation of the clinical condition of the patient at the time Slater examined him.

RESULTS

Table 1 presents the Phillips premorbidity ratings for each male twin in the sample.

Three main points brought out by Table 1 need to be considered.

1. Our first hypothesis leads us to predict that the premorbidity scores of the discordant index cases will be lower than the scores of the concordant index cases or the scores of all concordant twins combined. Although the mean premorbidity scores are rather high (poor) for both the concordant and the discordant schizophrenic twins, there is a slight difference of 2.9 scale points in favor of the discordant schizophrenic cases ($t = 2.531$, $P < .05$). Despite the fact that this finding accords with the prediction, there is not a single case among the discordant index cases which would be classified as a premorbid "good" (a score of 14 or less) by the Phillips Scale.

We can say that a relationship between premorbid adjustment and concordance or discordance among the monozygotic twin pairs appears to be indicated by the data. We are not able however to draw any inferences from these data about genetic differences between process and reactive schizophrenia since reactive types, as reflected

by good premorbid scores, do not occur in the sample at all. To test for such a difference, it may be necessary to find monozygotic twin index cases who are clearly of the reactive type and: a) see if their cotwins more often are free of schizophrenic illness than are the cotwins of process type cases; or b) see if the cotwins of both types of index cases are concordant with respect to these types.

2. Why is there an absence of reactive cases in the sample? Does reactive schizophrenia occur only rarely among one-egg male twins? There are no data available to suggest that its occurrence is less frequent among such twins than in the population generally. Unfortunately, we have no satisfactory information about what the proportion of reactive to process cases is in a population of newly hospitalized schizophrenic subjects. In any event, the sample seems to be biased in favor of process-type cases. One may wonder if such a bias may not creep into other twin studies when sampling is not even more rigorously controlled.

3. If we examine the discordant twin pairs, we see that in each instance where the twins could be differentiated on this scale, the twin who had the better premorbid social and sexual history was the one who escaped the illness. The scores of these twins tend to be in the middle range of the scale, except the cotwin in Case 133, whose low score is based on his statement that he had married and sired a child, though his sister doubted this. If we had disallowed his own report, his score would also have been in the middle range. Unfortunately, in two of the six pairs not enough information was available to differentiate the twins. Even so, a Mann-Whitney U test indicated that the two groups were reliably differentiated by the Phillips Scale ($U = 4.5$, $P = .017$). Thus, there is a suggestion that whether or not a twin among the discordant pairs developed schizophrenia seemed to be more closely associated with his premorbid history than with his genotype.

TABLE 2

Age of First Admission for Schizophrenia of the Affected Monozygotic Male Twins

Concordant pairs			Discordant pairs	
Case #	Index case	Cotwin	Case #	Index case
30	17	22	61	45
80/174	27*	28*	133	35
87	17	never hospitalized suicide, 28	202	38
240	27	29	231	29
287	25	26	17	40
			160	39
Sum	113	105	Sum	226
$\bar{X}$	22.6	26.25	$\bar{X}$	37.7
S.D.	4.29		S.D.	4.89

* Both twins were index cases. See footnote‡, Table 1.

Our second hypothesis is that the severity of the illness is greater in concordant than in discordant twins. More specifically, it was predicted that the disease would have an earlier "onset" and worse outcome for the concordant twins. Time of onset is notoriously difficult to pinpoint in any given case, but for purposes of group comparison, age at first admission for the illness is perhaps the best objective indicator of earliness or lateness of onset. Following the suggestion from Table 1 that the male concordant and discordant pairs may be genotypically different, we analyzed age at first admission and subsequent data separately for the male twins.

From Table 2, it is clear that the concordant male twins were hospitalized much earlier than the discordant male twins, the means being 24.2 years vs. 37.7 years. There is virtually no overlap of the two groups. The mean age difference is 13.5 years, which is significant at well beyond the .001 level.

The clinical condition of each patient at the time of examination is described by Slater in fair detail. Key phrases by Slater summarizing "outcome" of the illness at this point in time are quoted in Table 3.

TABLE 3

Clinical Outcomes of the Schizophrenic Illness for the Concordant and Discordant Monozygotic Male Twins

Concordant pairs			Discordant pairs	
Case #	Index case	Cotwin	Case #	Index case
80	"motionless lump"	"deteriorating"	61	"no evidence of gross affective dementia or . . . thought disorder."
80/174	"manneristic, suspicious" AWOL, stayed home	"deterioration steady and extreme"		
87	"deteriorated"	never seen by Slater	133	"well-preserved"
			202	"coherent; clearly orientated; memory preserved"
240	"malignant"			
	"incoherent, gross thought disorder"	"deteriorated"		
			231	"well-preserved"; discharged; working
287	"fairly normal"; married, working	"schizoid"; partly employed by father, at home	17	"remarkable preservation of personality"; discharged; not working
			160	"almost completely deteriorated"

If we describe these outcomes as simply "good" or "poor," the latter term covering deteriorative outcomes, the former nondeteriorative, six of the nine rateable concordant twins had a poor outcome as compared to one of the six discordant twins. Fisher's exact probability test yields a p-value of .078, which falls barely short of the usually accepted .05 criterion of significance.

It thus appears that the hypothesis of a more severe illness in the concordant than discordant male twins has considerable support in these data. Because of these differences, it seemed worth inquiring into the Kraepelinian subtype diagnoses of all the affected twins, insofar as such diagnoses could be estimated.

Slater reports that in all concordant uniovular twins, male and female, only one twin was without catatonic signs and symptoms, and it appears from Table 4 that the concordant male twins were predominantly in the catatonic subgroup while the discordant male twins were primarily paranoid.[4]

Our third hypothesis led us to predict that we would find a higher incidence of schizoid-schizophrenic illness in the families of the concordant than of the discordant pairs.

According to Table 5, four of the five families of the concordant pairs have a markedly schizoid member, or a member whose illness is probably schizophrenic, but no such cases are found in the families of the discordant pairs. The nephew of Case #17 had been admitted to a psychiatric clinic at age 18 with paranoid schizophrenia, but Slater states that some clinical signs suggested pituitary abnormality from which the patient had recovered, and he had remained well for the 25 years since. The higher incidence among the families of the concordant twins cannot be due to a greater number of relatives in these families, since there were 24 siblings of the discordant pairs

[4] Of course, these are mostly chronically ill patients who do not represent the entire range of catatonic and paranoid subtypes. Clearly, there are acute and intermittent catatonics whose course is generally more favorable than that found in the concordant twins, as well as a fairly large group of acute paranoid patients whose course leads to deterioration. Neither hebephrenic nor simple schizophrenia is represented in this group of subjects. A larger sample may have included a wider range of subtypes.

TABLE 4

*Suggested Subtype Diagnoses of the Concordant and Discordant Monozygotic Male Twins**

Concordant pairs			Discordant pairs	
Case #	Index case	Cotwin	Case #	Index case
30	(S) Catatonic	Mixed, catatonic and paranoid	61	Paranoid, with depressive features
80/174	Mixed, predominantly catatonic with paranoid features		133	(S) Paranoid, or, schizo-affective with manic-depressive type mood swings.
87	(S) Catatonic	Not diagnosable		
240	(S) "Mainly catatonic"		202	Paranoid
287	Paranoid, with catatonic features		231	(S) Paranoid
			17	(S) Paranoid
			160	Predominantly paranoid initially, before deterioration

* Where Slater had indicated a diagnosis made by the hospital at admission or reevaluation, or by himself based on his own examination, that diagnosis has been preceded by the symbol (S). The remaining diagnoses are suggested by the author as a best estimate, based on the descriptions provided.

TABLE 5

Incidence of Schizophrenic Illness in the Families of the Monozygotic Male Twins

Case #	Concordant pairs	Case #	Discordant pairs
30	Sister, markedly schizoid, socially withdrawn	61	None
		133	None
80/174	Mother shared some of son's delusions	202	None
		231	None
87	Maternal aunt died in mental hospital	17	Nephew, once diagnosed as paranoid schizophrenic, but called "pituitary disturbance" by Slater.
240	Grandfather, "religious mania," in mental hospital till death		
287	None	160	None

who survived to a susceptible age as compared to only 11 such siblings of the concordant pairs. Other kinds of psychiatric disturbances occurred with high frequency in the families of both concordant and discordant pairs. These included mental deficiency, alcoholism, psychopathy, neuroses such as anxious-phobic states and reactive depression, and personality problems such as diffidence, excessive worrying, etc.

Although we cannot make premorbidity ratings for the female twins, we can test hypotheses 2 and 3 with these cases. In this regard, the first point of note is that whereas there were only 11 pairs of monozygotic male twins in the sample, there were 26 pairs of female twins. Of the 11 male pairs, five were concordant. Of the 26 female pairs, 19 were concordant. These differences are striking and raise the question of whether we are dealing here with sampling errors or real differences. Actually, there is a large variety of studies which contain a higher number of female index cases and higher concordance rates among females with regard to mental illness. It would take us too far afield to review these studies here, but they appear to throw additional light on the question of hereditary vs. life-experience factors in schizophrenia.

Since the N is so large, we will not set up tables for the female pairs as we did for the males. We may summarize the findings briefly by stating that the hypothesis of

TABLE 6
Incidence of Schizophrenic Illness in Families of the Concordant and Discordant Monozygotic Pairs: Both Sexes

	Family history positive for probable schizophrenic illness	Family history negative for probable schizophrenic illness
All concordant pairs	13	9
All discordant pairs	1	12

greater severity of illness in the concordant than in the discordant twins finds no support in the data, whereas the hypothesis of higher incidence of schizophrenia in the families of the concordant pairs finds additional support. The mean age at first hospitalization was 31.72 years for the concordant female twins, 33.14 years for the discordant female twins. The difference is not noteworthy. With respect to outcome, 14 of 34 rateable concordant female twins were said to be deteriorated as compared to four of the six rateable discordant female twins. The difference is not statistically significant but is actually in the opposite direction from that predicted.

These findings reinforce opinions stated in the past that there are striking differences in the clinical conditions of male and female schizophrenic patients, and that females are less predictable. Similarly, whereas a premorbidity scale to predict outcome of illness in schizophrenic males could be constructed fairly easily, one has yet to be worked out which will as reliably predict outcomes with schizophrenic females. Thus, when dealing with clinical phenomena, it is judicious not to pool the sexes.

Of the 19 concordant female pairs, histories of probably schizophrenic illness occurred in nine families, absence of such history occurred in eight families, and in two families there was sufficient doubt about a case to defer a definite classification. Of the seven discordant female pairs, absence of schizophrenic history was noted in six families. In the seventh family, one relative was said to have had a schizophrenic episode at age 19, recovered in short order, and to have been well since. If we pool the family incidence figures for both sexes, we find the distribution shown in Table 6.

It can be seen from Table 6 that the families of the discordant pairs are virtually free of schizophrenic illness. In the one case where the illness is said to have occurred, the course was unusually rapid and benign. By contrast, about 60 per cent of the families of the concordant pairs showed evidence of a schizophrenic illness. Testing the significance of the difference, we find a chi-square, corrected for continuity, of 6.98, which is significant at well beyond the .01 level.

DISCUSSION

Our analysis provides support for the hypothesis of biological heterogeneity in schizophrenia. On the one hand, the combined findings of discordance in monozygotic twins and the virtual absence of schizophrenia among members of their families are strongly suggestive that a schizophrenic gene is not the responsible agent in the illness of these twin index cases. For the male twins we may specify even further that the illness is more closely linked to the type of premorbid social and sexual history that the twin experienced than to his genotype. We may state too that the type of illness in males in which genetic factors are of minimal or no importance is one which has a relatively late onset and benign outcome in that the illness does not progress to deterioration and is manifested clinically as a predominantly paranoid syndrome, sometimes accompanied by prominent affective features.

On the other hand, the combined findings of concordance in the monozygotic twins plus the fact that history of probable schizophrenic illness occurs in approximately 60 per cent of their families is strongly suggestive of an hereditary determinant. Of the

male twins we may add that genotypic expression is manifest early in that these patients have both a poorer premorbid social and sexual history and a relatively early onset of the disease. Moreover, the illness tends to be malignant, with a preponderance of catatonic symptoms.

Evidence of biological heterogeneity with respect to the paranoid and catatonic subtypes can be found in the data of Kallmann (6) and Zehnder (21), as pointed out by Slater (19). Our findings suggest that the relationships found in these studies could be made clearer still if the cases were analyzed separately by sex, and if, among the male paranoid schizophrenics, those who had a relatively late onset and benign outcome were separated from the other patients included in this subtype.

There is also evidence, in keeping with our findings, that genetic factors play a differential role with respect to course and outcome of the disease. Slater (19), analyzing the sibling pairs of Zehnder, who had classified their outcomes as "dementia, chronicity, or remission," found a positive relationship between brothers and sisters in this respect. Slater (20) grouped together all concordant uniovular twins, binovular twins, and sibling pairs, and also concluded that genetic factors helped to determine whether the illness took a relapsing form or not. Luxenburger (10) had already noted a tendency for the end-state of schizophrenic illness in concordant monozygotic twins to correspond, especially in the hebephrenic and catatonic forms of the disease as compared to the paranoid or mixed forms.

Some inconclusive evidence also exists to show that concordance with respect to age of onset of schizophrenia is greater when the hereditary relationship is closer. Thus, Luxenburger (11) has presented tables which, analyzed statistically, show that uniovular twins have a more similar age of onset than siblings, and siblings a more similar age of onset than a selected sample of unrelated cases. Slater (20) also found a higher correlation between concordant one-egg twins with respect to age of onset than between concordant sibs, although for two-egg twins the correlation was higher than for one-egg twins.

The latter apparent contradiction suggests that the contribution of non-hereditary factors to an aspect of the illness such as age of onset may be considerable. Neither can such factors be ruled out with respect to clinical subtype and outcome of the illness, but the case for genetic determinants in these respects is somewhat stronger.

Two matters of moment which must be considered even more seriously are sampling procedures in twin studies of psychiatric illness and male-female differences with respect to such illnesses. Each of these problems merits separate review in a manner too detailed to attempt here.

In a recent provocative article, Anastasi (2) has pointed out that the heredity-environment controversy is far from dead, although some scientists may have wished long since to bury it. Rather, she has suggested, if we ask the right questions, and are skillful enough in applying techniques of study and analysis, our body of knowledge about many fundamental matters may be enriched considerably. It is in this spirit that the present study has been undertaken.

SUMMARY AND CONCLUSIONS

This study addresses itself to the question of biological unity in schizophrenia. The case histories of monozygotic twins published by Slater (20) are analyzed with respect to three hypotheses. There is almost a total absence of schizophrenia in the families of the discordant twin pairs, but the illness occurs in about 60 per cent of the families of the concordant twin pairs. The affected discordant male twins tend to have a later age of onset and more favorable outcome than the concordant male twins. The former tend to be of the paranoid subtype, the latter catatonic. Of the discordant male twins, the one who does not become ill tends

to have the better premorbid social and sexual history, and the twin who does become ill tends to have a better premorbid adjustment than do the concordant twins. It is concluded that, biologically speaking, at least two broad groups of schizophrenia are differentiated by this method of analysis: in one, the genetic contribution is absent or minimal; in the other, the genetic contribution is probably considerable.

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