Brit. J. Psychiat. (1965), **111**, 1119–1120

Correspondence

GENETICS OF SCHIZOPHRENIA

DEAR SIR,

In the current discussion concerning the genetics of schizophrenia it should be remembered that mendelian genetics is a formal science and that for a particular scheme of inheritance, and given allelic frequencies, familial relations are automatically defined. In practice, the predictions from the simplest mendelian assumptions sometimes require modification to allow for such complications as selection effects, differential fertility, linkage, and gene mutation. Where diseases such as schizophrenia are concerned, interpretation of the familial evidence is further complicated by the problems of diagnosis and the variation of penetrance with age and to some extent with sex. Consider, however, the simple mendelian relation between the twins evidence and that concerning full sibs. Suppose the age- and sex-corrected concordance-rate of schizophrenia in monozygotic twins is S_M, and that in dizygotic twins it is S_D. Then, in a proband study, if one member of a family is a proved schizophrenic, the proportion of full sibs that will be *genetically predisposed* to schizophrenia should, on the average, be : S_D/S_M. For the five major twins studies analysed by Essen-Möller (1963) this ratio is approximately $0{\cdot}18_8$. (It should be noted that this ratio is too small to be accounted for by any straightforward monogenic scheme of inheritance.) The observed *risk* in full sibs is $0{\cdot}11_5$ to $0{\cdot}14_3$, corresponding to average penetrances of about 61 to 76 per cent. This, and other familial evidence, is consistent with the hypothesis that predisposition to schizophrenia is governed by recessive inheritance at two autosomal loci (Burch, 1964). Furthermore, the sex- and age-distributions of schizophrenia as diagnosed in New York State, 1949 to 1951, indicate that the predisposed sub-population is homogeneous with respect to the two random, dependent-type events that appear to initiate the disease process (Burch, 1964). The high degree of internal consistency in the earlier evidence—including the extensive familial studies by Kallmann—strongly supports the genetic hypothesis. The critical analysis of Shields (1965) suggests that Tienari's (1963) subsequent twins study does not vitiate this hypothesis.

I recently proposed (Burch, 1964) that schizophrenia is either a spontaneous disturbed-tolerance autoimmune disorder involving cell-bound (lymphocytic) autoantibody as the primary pathogen, or that it arises from spontaneous disturbances in an unidentified system that shares certain important genetical and statistical characteristics with the lymphoid system. On basic biological grounds described in detail elsewhere (Burch and Burwell, 1965) I now consider that the autoimmune interpretation is the more plausible.

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DEPRESSION : PSYCHOTIC/NEUROTIC ; ENDOGENOUS/EXOGENOUS

DEAR SIR,

Carney, Roth and Garside (*Journal*, Aug. 1965, p. 659) conclude that the separation of *endogenous* and *neurotic* depression is possible and useful ; Mendels (*Journal*, Aug. 1965, p. 682) seem to regard it as neither possible nor useful.

Mendels claims that his results "lend support to the concept that there is always an endogenous element to depressive illness, and that the reactive element is more variable". Since the terms endogenous and reactive are exhaustive, this must mean that all reactive depressives are endogenous, but not all endogenous depressives are reactive. The distinction has, therefore, been made, but in terms of a "contained within" relationship.

The facts are not, however, supportive of this view. Table II (p. 685) can serve as the crux of the argument. In this Table the figures are given inaccurately, assessed incorrectly and interpreted arbitrarily.

Under A/E, all 11 subjects had a Steady Course; but 1 must have had a Fluctuating Course as well. Under B/E, 18 out of 19 subjects had an Adequate

premorbid personality and 2 had an Inadequate personality. One must, therefore, have had both. Under B/R someone had no personality at all.

Mendels claims that none of the features of endogenous depression occur dominantly in that group. The first one I tried out—Psychomotor Retardation—was significantly commoner among endogenous depressives (under B/EvR, Chi Squared is 6·7 for 1 df). Others look significant.

"Those symptoms which occur predominantly in one syndrome are : emotional lability . . . (and four others) . . . They have all been used as features of reactive depression." But one cannot demonstrate that emotional lability predominates significantly in reactives without showing that the absence of lability predominates in endogenous depressives. Adequate personality and Steady Course are used under endogenous and their opposites under reactive. This is inadmissible and renders Mendel's interpretation arbitrary.

The weight of the evidence lies, therefore, with Carney *et al.* It is unfortunate that they chose terms from two different universes of discourse.

G. A. Foulds

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SLEEP PATTERNS IN REACTIVE AND ENDOGENOUS DEPRESSIONS

Dear Sir,

In his letter (*Journal*, Aug. 1965) bearing the above title, Abrams seems to be inviting Costello and Selby to use the Early Waking as a cardinal symptom for the diagnosis of endogenous depression, when he feels sure they would find that Early Waking was commoner in endogenous depression. I am sure he is right.

"When a clinical psychiatrist examines a patient for the first time he is surely not aware of the diagnosis." But he may quite soon form an impression. If this impression is Endogenous Depression, he may press home questions relating to early waking ; if the impression is Reactive Depression, he may not ask the question with the same persistence. It would further appear that the "well-known clinical observations" have failed to take account of the correlation between ageing and early waking amongst normal people (McGhie and Russell, 1962) and amongst Depressives (Foulds, 1960). I am at the moment on holiday in Minorca ; I am not feeling at all depressed, but I do experience early waking. This I attribute to taking a siesta after lunch. Endogenous or Reactive?

G. A. Foulds

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AN OMISSION

Dear Sir,

In my article "Electroconvulsive Therapy and Depression" which appeared in the *Journal* for August, 1965, the following acknowledgment was inadvertently omitted:

> "I am grateful to Professor L. A. Hurst and Dr. H. Moross for their generous provision of facilities to conduct this study; and to the medical staff of Tara Hospital, Johannesburg, who allowed free access to their patients. I am also grateful to Professor J. E. Kerrich, who advised on statistical procedures and Dr. D. Henderson and Miss Kay Krige of the University of the Witwatersrand Computer Center for their assistance with the programming."

I am taking the opportunity of remedying this and of apologizing to those concerned.

J. D. Mendels

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