

Original Articles

A Note on “Survey of Cases of Familial Mental Illness” by L. S. Penrose

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Received July 30, 1990

The following paper is a report submitted in 1945 by L. S. Penrose to the Division of Psychiatric Research, Ontario Department of Health concerning a study of the familial incidence of mental illness that he had recently completed. Some years ago I was given a mimeographed copy by G. Winokur, who I believe had received it in earlier correspondence with Penrose. As far as I am aware this paper (referred to in Penrose's bibliography (Harris 1973) as a report to the Ontario Department of Health) has never been published, although it is clear that Penrose abstracted material from it some years later in a chapter entitled “Critical Survey of Schizophrenia Genetics” (Penrose 1968).

The paper has a number of points of interest. Although dependent upon hospital diagnoses, the material is systematically collected and the sample size is large. It may be objected that (with recent operational criteria) diagnostic boundaries might now be drawn with greater objectivity and otherwise located, but it is as yet unclear that such criteria are more valid. The comparisons that Penrose made between groups and between different familial relationships are not obviously outdated by subsequent developments. No other comprehensive and hospital-based studies appear to have been conducted and analysed in quite the same way.

Two aspects I found of particular relevance to my own interests:

(i) The possible genetic relationship between schizophrenia and affective illness to which Penrose draws attention in Table 5 and in point (i) of the summary is of relevance to recent concepts (e.g. Crow 1990) of a continuum of psychosis. Later Penrose (1968) discussed such a concept and also the question of whether age of onset might be a better and more reliable defining characteristic than clinical presentation.

(ii) The tendency for affected relatives (particularly siblings) to be more often than would be expected of the same sex. In an earlier discussion, Penrose (1942a) included “auxiliary” genes that play a part in sex determination as “contributing causes” of mental illness. Another explanation (Crow 1988) is that a gene for psychosis is located in the pseudo-autosomal region of the sex chromosomes. Whatever the explanation, the data presented here, in that they constitute a large and systematically collected series, are perhaps the most convincing evidence for the reality of the finding. The excess of relatives of the same sex is present for both male and female probands and for schizophrenic and affective illness [point (vii) of the Summary]. This finding, first noted by Mott (1910) and discussed by Rosenthal (1962), may be an important clue to the nature of the genetic contribution to psychosis.

Other points deserve attention. In sect. 2 paragraph 2, Penrose writes that “Relative rarity of schizophrenia in male parents is an important feature which permeates the whole survey... the same feature shows itself clearly, when age on first admission to hospital is analysed, in the fact that mental illness of early onset is rare in fathers.” Elsewhere Penrose (1942b) discussed the possible evolutionary significance of age of onset and sex differences in psychosis.

On p. 7 Penrose draws attention to “an extra peculiarity... in the fact that, whereas schizophrenic fathers have more psychotic sons than psychotic daughters (41:31), schizophrenic mothers have fewer psychotic sons than psychotic daughters (109:113). The counterpart of this, for parents with affective psychosis, is that fathers diagnosed affective have fewer psychotic sons than psychotic daughters (136:146), whereas mothers diagnosed affective have more psychotic sons than psychotic daughters (191:148)”. Analysed in terms of diagnosis in the child (Penrose 1968) there is a surprising excess of children with a diagnosis of schizophrenia, of parents with a diagnosis of affective disorder. In Table 8 it can be seen that there is also a relative lack of affectively ill sons of affectively ill fathers (that has sometimes been cited in support of X-linkage in the affective disorders), and a relative excess of sons with schizophrenia and of daughters with affective disorder, when the mother suffers from affective illness. The meaning of these relationships is as yet unclear, but perhaps is more likely to be discernible when, as Penrose had arranged, data for the whole range of psychotic illness is included.

In discussing correlations in age of onset Penrose writes (sect. 4 paragraph 6) that, “The relatively low values of the parent-child and grandparent-grandchild co-efficients, as opposed to expected values of 0.500 and 0.250, respectively,

for multiple additive factors, taken together with the high values of sib-sib, uncle-nephew, aunt-niece etc., co-efficients suggest strongly that some of the multiple factors are recessive genes” and in the next paragraph, concerning the differences between the co-efficients for paternal and maternal uncles and aunts and nephews and nieces, that “These findings are in keeping with what would be expected if one or more of the genetic factors which modify age of onset were sex-linked . . .”.

The suggestions that sex-linked and recessive genes are responsible for aspects of psychosis are amongst the reasons why it seems that the data collected and analysed by Penrose ought to be more widely known.

Acknowledgements. I am grateful to G. Winokur for drawing my attention to the existence of Penrose’s report and for supplying me with a copy and to L. S. Penrose’s daughter, Dr. Shirley Hodgson, for her agreement that the report be published.

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Survey of Cases of Familial Mental Illness¹

L. S. Penrose, July 1945

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1 Introduction

The material presented here summarizes an investigation undertaken by the Division of Psychiatric Research. There were two main objects in view, both connected with the study of the constitutional background of mental illness. First, the nature of familial mental illness was examined with respect to psychiatric diagnosis; that is to say, the question was asked: if a close relative of a patient breaks down into mental illness, how far will this illness in the relative resemble that of the patient clinically? The information of this kind obtained by examining records of patients admitted to the Ontario Hospitals gives clues as to how far certain mental illnesses are or are not genetic entities. Secondly, in consequence of the unreliability of clinical diagnosis, a complete analysis was made of the ages of onset of patients compared with those of their mentally ill relatives without reference to the type of illness. The age of onset was measured by taking the date of first admission to any mental hospital. Though it was, of course, realised that the admission date only approximately represents the age at onset of illness, this date is highly correlated with the beginning of acute symptoms and has the advantage of being an exact measurement. As will be shown in Sect. 3, the age

at first admission is a characteristic feature of each separate type of illness diagnosed. Furthermore, because it is an arithmetic criterion, the age at first admission can be used in calculations to estimate the likeness of type of illness in different relatives. From these measurements, information can be obtained about the mode of inheritance of the factors that determine either the mental illness itself or of the constitution which predisposes to such illness.

The survey, which was begun in 1943 at the Ontario Hospital, London, was continued first at Queen Street and then further extended to cover all the Ontario Hospitals. The families in which more than one relative had been admitted were traced through the patients’ statistical cards. These records go back to 1926, and thus, a period of at least 18 years was covered. Files of all cases selected in this manner were searched, and a great many special enquiries were made. Only those instances where at least one member of the family was diagnosed as mentally ill were included; that is to say, cases of uncomplicated mental defect did not come into the survey unless a relative had mental disorder. The survey, moreover, was limited to patients who had actually been resident in mental hospital at some time during their lives, with one exception, namely, cases where a relative had committed suicide were also included in the survey. In such instances, the data of suicide of a subject who had not been admitted to a mental hospital was taken as being equiva-

¹ Stylistic amendments to the original Penrose text have been made where necessary for further clarity