Evaluating the Spectrum Concept of Schizophrenia in the Roscommon Family Study

Kenneth S. Kendler, M.D., Michael C. Neale, Ph.D., and Dermot Walsh, M.B., F.R.C.P.I.

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Objective: The authors sought to evaluate whether the pattern of schizophrenia and related disorders in probands and their relatives can be explained by a single underlying continuum of liability to the "schizophrenia spectrum." Method: In the epidemiologically based Roscommon Family Study, the authors separately examined—in siblings, parents, and relatives of index and comparison probands—the familial aggregation and coaggregation of five hierarchically defined disorders: schizophrenia, schizotypal disorder, schizotypal/paranoid personality disorder, other nonaffective psychoses, and psychotic affective illness. A multiple threshold model was fitted to these contingency tables by maximum likelihood. Results: The multiple threshold model that constrained resemblance to be the same in siblings and parents fit the data well and estimated the correlation in liability to schizophrenia spectrum disorders between probands and first-degree relatives at 0.36. Parents, however, required higher levels of liability to manifest schizophrenia spectrum disorders than siblings. While schizophrenia and psychotic affective illness could be clearly assigned to the two extremes of the schizophrenia spectrum, the proper ordering of schizoaffective disorder, schizotypal/paranoid personality disorder, and other nonaffective psychoses could not be unambiguously determined. Conclusions: These results are consistent with the existence of a schizophrenia spectrum in which these five disorders are manifestations, of varying severity, of the same underlying vulnerability. This vulnerability is strongly transmitted within families.

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If one observes the relatives of our patients [with schizophrenia], one often finds in them peculiarities which are qualitatively identical with those of the patients themselves, so that the disease appears to be only a quantitative increase of the anomalies seen in the parents and siblings.

—E. Bleuler (1, p. 238)

Although the concept of the “schizophrenia spectrum” has been widely used only since the publication of the landmark Danish Adoption Study of Schizophrenia (2, 3), its historical roots can be traced back to the beginning of modern psychiatry (4). In the eighth edition of his influential textbook, Kraepelin noted that many “striking personalities” of the relatives of schizophrenic patients probably had the same “principal malady” as their more overtly ill relative (5). Bleuler made similar observations (such as the opening quotation) (1). In the first major family study of dementia praecox, Rüdin observed that siblings of ill probands had an excess not only of schizophrenia but also of a variety of other psychotic disorders (6). In describing one of the classic family studies of schizophrenia, Kallmann wrote of the “group of schizoform abnormalities” and the “schizophrenic disease-complex” (7).

While widely used, the hypothesis of a schizophrenia spectrum has rarely been subjected to formal evaluation. Numerous studies have found that relatives of schizophrenic probands are at greater risk for a range of psychiatric disorders (6, 8-10). However, we are aware of only two studies (11, 12) that have evaluated the central postulate of the schizophrenia spectrum: that a range of disorders of varying severity share with schizophrenia the same underlying familial vulnerability. These two studies reached contrasting conclusions, with one supporting (11) and the other rejecting (12) the schizophrenia spectrum hypothesis. Both of these
studies had potentially significant methodological limitations such as small sample size (11), limited assessment of schizophrenia spectrum personality disorders in relatives (12), and a narrow range of proband diagnoses (11, 12).

In this report, we address the validity of the underlying hypothesis of the schizophrenia spectrum by examining, in the Roscommon Family Study (13), the pattern of familial aggregation and coaggregation of five psychiatric disorders that form a putative schizophrenia spectrum: schizophrenia, schizoaffective disorder, schizotypal/paranoid personality disorder, other nonaffective psychoses, and psychotic affective illness. These disorders were chosen because of evidence both from previous investigations (8–12, 14) as well as the Roscommon Family Study (13, 15–17) that they share familial vulnerability factors with schizophrenia. Of note, the Roscommon Family Study contains epidemiologically ascertained probands from all five of these diagnostic categories.

METHOD

Sample and Diagnostic Assessment

Based in a rural county in western Ireland, the Roscommon Family Study contained three proband groups: 1) “schizophrenic”—all subjects with a diagnosis of schizophrenia from the Roscommon County Case Register (N=303) (18), 2) “affective”—a random subsample of 75% of the case register subjects with a diagnosis of major affective disorder (N=99), and 3) comparison subjects selected from the county electoral registry (N=150) who were age- and sex-matched to the schizophrenic and affective proband groups (13). We attempted to personally interview all probands and, blind to proband status, their first-degree relatives in Ireland, Northern Ireland, and central and eastern England. We also obtained and abstracted all available psychiatric records for hospitalized probands and relatives. Some probands and relatives were ascertainment more than once. To obtain the correct risk in relatives, we used the general proband method in which all individuals are counted once for each time they are independently ascertainment (19). This study was approved by the Health Research Board, Dublin, which was consistent with research practice in the Republic of Ireland, permitted the use of verbalassen rather than written consent for studies limited to personal interviews. All individuals interviewed in this project gave verbal assent to their participation.

Personal interviews were completed for 88% of living traceable probands (N=415) and 86% of living traceable relatives (N=1,753). These interviews used an adapted version of the Structured Clinical Interview for DSM-III-R (20) for axis I disorders and the Structured Interview for Schizotypy (21) for schizophrenia-related axis II disorders. Hospital records were obtained and abstracted for 181 relatives. Our analyses are restricted to relatives with a personal interview or hospital record.

Blind, best-estimate DSM-III-R diagnoses that used all available information were made for all probands and relatives by one of us (K.S.K.) or Alan M. Gruneberg, M.D.; there was high interrater reliability (13). Diagnoses were made at three levels of certainty. We report here only those analyses based on the broad criteria of definite, probable, or possible cases. Psychotic probands in the Roscommon Family Study had few children. Therefore, the present analyses are restricted to full siblings and parents. Previous evidence (22) and the findings from the Roscommon Family Study (13) indicate that schizophrenia as well as other psychotic disorders are associated with a significant reduction in reproductive fitness. As initially demonstrated by Essen-Möller (23), and elaborated by others (24–26), the effects of a disorder on reproductive rates can substantially influence the pattern of risk of that illness in relatives and will produce qualitatively different effects in siblings and parents. Therefore, in these analyses, siblings and parents are analyzed separately.

We examined five diagnostic categories based on DSM-III-R criteria that, from previous results in the literature (8–12, 14) as well as prior morbidity risk analyses in the Roscommon Family Study (13, 15–17), might form in the following a priori order a putative schizophrenia spectrum: 1) schizophrenia, 2) schizoaffective disorder, 3) schizotypal/paranoid personality disorder, 4) other nonaffective psychoses (schizophreniform disorder, delusional disorder, or atypical psychosis), and 5) psychotic affective illness.

In addition, we analyzed the original comparison group. Any individual with two or more of the relevant diagnoses was assigned for these analyses to the diagnosis that is higher in the hierarchy. The age of parents of the subjects in the six proband groups did not differ significantly. While there were significant differences among the groups in age of the siblings, these differences were due to the siblings of probands with psychotic affective illness whose age (mean=46.9 years, SD=14.2) was around 4 years older than that of siblings of the other proband groups (e.g., the mean age of the siblings of schizophrenic probands was 42.5 years, SD=11.8). This difference was judged too small to warrant the introduction of the complexities of age correction into our analyses.

Sample sizes of probands, siblings, and parents, respectively, of these six groups were as follows: schizophrenia—102, 264, and 80; schizoaffective disorder—34, 112, and 29; schizotypal/paranoid personality disorder—16, 39, and 14; other nonaffective psychoses—34, 98, and 25; psychotic affective illness—53, 144, and 36; and comparison—122, 393, and 98.

Statistical Methods

In the Roscommon Family Study, comparison probands were a random sample from the population, matched to the index probands for age and gender. Since these comparison subjects were not “super-normal” (i.e., individuals were retained even if they manifested schizophrenia or related disorders), we were able to estimate the population proportions of each of the schizophrenia spectrum disorders. The same estimation of proportions cannot be done with the index probands alone because the probability of hospitalization varies with the particular disorder (e.g., those with schizotypal personality are much less likely to be hospitalized than those with schizophrenia). Therefore, we need to analyze the data from the hospital and comparison probands jointly but not let the disproportionate representation in the hospital cohorts bias the estimates of population prevalence. We assume that those subjects hospitalized with the disorder are representative of their particular disorder subgroup, i.e., that there is no relationship between probability of hospitalization and liability within each diagnostic category. Therefore, we can tackle the problem analytically by considering the data as samples from six independent groups: the comparison probands and one group for each diagnostic category of the ill probands. Data from the comparison subjects and their relatives are summarized as two 6×6 contingency tables (one for siblings and one for parents), whereas the data on ill probands and their siblings and parents are summarized in two series of 1×6 tables. These raw contingency tables are available from Dr. Kendler.

We assume that the data from multiple siblings within the same family are statistically independent. While not precisely correct, previous simulations suggest that this will have little practical effect on our results (27).

The Multiple Threshold Model

The multiple threshold model (28) assumes that all of the disorders in the putative schizophrenia spectrum are influenced by the same underlying liability or vulnerability. The disorders differ, however, in the severity of that liability. On average, individuals with schizophrenia will have higher liability than, for example, individuals with schizotypal personality disorder. The key assumption of the multiple threshold model, then, is that with respect to the underlying liability to illness, the disorders in the schizophrenia spectrum differ quantitatively but not qualitatively.
We assume a continuous, normal distribution of liability to schizophrenia spectrum disorders with a series of abrupt thresholds that mark the boundaries between the ordered categories of the schizophrenia spectrum. Because we are examining pairs of relatives between whom we expect a correlation in this underlying liability to illness, we can predict the expected pattern of risk of disorders from the placement of the thresholds, the degree of correlation, and the properties of the normal bivariate distribution.

For the comparison data, this procedure is standard for estimation of a polychoric correlation. In the proband data, the bivariate normal density function is corrected for ascertainment in each 1X6 table, so that the predicted cell proportions sum to unity within each group. This procedure is automatically invoked when cells are marked as missing in Mx (29).

**Model Fitting**

Model fitting was performed by using the program Mx (29), which, along with documentation, may be obtained through anonymous binary file transfer protocol (ftp). The internet address is opal.vcu.edu; the file is in directory /pub/mx (or with a www browser access “http://opal.vcu.edu/html/mx/mxhomepage.html”). Neale and Cardon (30), Lochlin (31), and Boelen (32) provided a general introduction to structural equation modeling. We begin by allowing the correlation in liability to schizophrenia spectrum disorders between probands and first-degree relatives to differ for siblings and parents and for each diagnostic category. We then constrain the correlations in liability between probands and relatives to be equal for all disorders and examine the deterioration in fit of the model. By so doing, we are formally evaluating whether the elevated risk of schizophrenia spectrum disorders in relatives of probands with each disorder is as predicted by the multiple threshold model. Next, we test the model by constraining the correlations to be equal in parents and siblings. Finally, we examine whether the threshold of illness can be assumed to be the same in parents, who must have successfully reproduced to be in our study, and siblings.

The goal of model fitting is to explain the observed data as simply as possible. To operationalize this, we used Akaike’s information criterion (33). This widely used fit index for covariance structure analysis performed the best of seven indices in a recent extensive simulation study in both frequently identifying the true model and rarely identifying false models (34). The model with the lowest (most negative) Akaike’s information criterion best combines the properties of explanatory power and parsimony.

**RESULTS**

In model I, the correlations in liability for the diagnostic classes between probands and first-degree relatives were allowed to differ across diagnostic classes and in siblings and parents. In addition, thresholds at which these disorders were manifest were allowed to differ in siblings and parents. Model I fit the data very well (Akaike’s information criterion=−124.5, \( \chi^2=71.5, df=98, p=0.98 \)).

The schizophrenia spectrum hypothesis predicts that the correlations in liability to schizophrenia spectrum disorders between probands and first-degree relatives should be equal for all the diagnostic classes. Model II tested this assumption by formally constraining all these correlations to be equal and produced a clear improvement over model I in the Akaike’s information criterion (−132.6, \( \chi^2=83.4, df=108 \)), thus supporting the hypothesis of a schizophrenia spectrum.

A further evaluation of this hypothesis was whether the correlation in liability between probands and first-degree relatives was the same for the parents and sib-

<table>
<thead>
<tr>
<th>Level</th>
<th>Disorder</th>
<th>Siblings</th>
<th>Parents</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Psychotic affective illness</td>
<td>1.64</td>
<td>1.71</td>
</tr>
<tr>
<td>2</td>
<td>Other nonaffective psychoses</td>
<td>1.79</td>
<td>1.90</td>
</tr>
<tr>
<td>3</td>
<td>Schizotypal/paranoid personality disorder</td>
<td>1.87</td>
<td>1.93</td>
</tr>
<tr>
<td>4</td>
<td>Schizofasic disorder</td>
<td>2.16</td>
<td>2.40</td>
</tr>
<tr>
<td>5</td>
<td>Schizophrenia</td>
<td>2.29</td>
<td>2.74</td>
</tr>
</tbody>
</table>

\( ^{a}\)Correlations in liability to schizophrenia spectrum disorders between probands and first-degree relatives are constrained to be equal for all disorders and for parents and siblings.

\( ^{b}\)Level refers to the severity of the disorder, based on an a priori hypothesis, with 1=least severe disorder and 5=most severe disorder.

lings of probands. Model III tested this assumption and resulted in no deterioration in fit from model II and a further improvement in the Akaike’s information criterion (−134.6, \( \chi^2=83.4, df=109 \)).

Finally, we examined whether the thresholds of the disorders could be constrained to be equal for parents and siblings. In model IV, we set equal only the threshold for schizophrenia and allowed the thresholds for the other disorders to differ. The fit of the model deteriorated substantially and produced a worse Akaike’s information criterion than model III (−131.5, \( \chi^2=88.8, df=110 \)). These results are consistent with previous evidence that the reduction in reproductive fitness seen in schizophrenia (13, 22) results in a substantially lower risk of illness in parents than in siblings of schizophrenic probands (23–26). In model V, we set the thresholds equal in siblings and parents for all disorders at once, with more equivocal results. The Akaike’s information criterion of model V was identical with that of model III (−134.6, \( \chi^2=93.4, df=114 \)).

Given that the threshold of manifestation for schizophrenia clearly differed in siblings and parents, we consider model III to provide the best explanation of the observed results. Table 1 shows the location (expressed in standard deviation units from the normal distribution) of the thresholds estimated by model III for the various disorders in siblings and parents. As expected, a more deviant liability is required to develop schizophrenia (≥2.29 standard deviation units above the mean in siblings) than, for example, schizotypal/paranoid personality disorder (≥1.87 standard deviation units above the mean). In addition, a higher liability is required for parents to manifest schizophrenia spectrum disorders than siblings. The correlation in liability to schizophrenia spectrum disorders between probands and first-degree relatives is estimated by model III as 0.36 with a 95% confidence interval of 0.30–0.42.

These analyses used our a priori order of diagnoses within the schizophrenia spectrum. The final series of analyses, summarized in table 2, tested the fit of other possible orders, assuming model III. The fit is given in chi-square units, in which a better fit is indicated by a smaller chi-square value.
TABLE 2. Fit of Multiple Threshold Model for Schizophrenia Spectrum Disorders as a Function of the Order of the Diagnostic Categories

<table>
<thead>
<tr>
<th>Order of Categories</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Psychotic affective illness</td>
<td>Other nonaffective psychoses</td>
<td>Schizotypal/paranoid personality disorder</td>
<td>Schizotypal/paranoid personality disorder</td>
<td>Schizotypal/paranoid personality disorder</td>
</tr>
<tr>
<td>B</td>
<td>Psychotic affective illness</td>
<td>Other nonaffective psychoses</td>
<td>Schizotypal/paranoid personality disorder</td>
<td>Schizotypal/paranoid personality disorder</td>
<td>Schizotypal/paranoid personality disorder</td>
</tr>
<tr>
<td>C</td>
<td>Psychotic affective illness</td>
<td>Other nonaffective psychoses</td>
<td>Schizotypal/paranoid personality disorder</td>
<td>Schizotypal/paranoid personality disorder</td>
<td>Schizotypal/paranoid personality disorder</td>
</tr>
<tr>
<td>D</td>
<td>Psychotic affective illness</td>
<td>Schizotypal/paranoid personality disorder</td>
<td>Other nonaffective psychoses</td>
<td>Schizotypal/paranoid personality disorder</td>
<td>Schizotypal/paranoid personality disorder</td>
</tr>
<tr>
<td>E</td>
<td>Other nonaffective psychoses</td>
<td>Psychotic affective illness</td>
<td>Schizotypal/paranoid personality disorder</td>
<td>Schizotypal/paranoid personality disorder</td>
<td>Schizotypal/paranoid personality disorder</td>
</tr>
<tr>
<td>F</td>
<td>Psychotic affective illness</td>
<td>Schizotypal/paranoid personality disorder</td>
<td>Schizotypal/paranoid personality disorder</td>
<td>Schizotypal/paranoid personality disorder</td>
<td>Schizotypal/paranoid personality disorder</td>
</tr>
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</table>

\[ \chi^2 (df=109) \]

\[ a \] Order of categories reflects severity of disorder, with 1=least severe disorder and 5=most severe disorder.
\[ b \] Model did not converge.

We began by switching each possible pair of adjacent disorders in the a priori order (see as model A in table 2). Model B, in which schizoaffective disorder replaced schizophrenia as the most severe disorder in the spectrum, fit considerably worse than the original model. However, models C and D, in which schizotypal/paranoid personality disorder was switched either with schizoaffective disorder or with other nonaffective psychoses, produced fits virtually the same as the a priori order. Model E, in which other nonaffective psychoses replaced psychotic affective illness as the least severe disorder in the spectrum, fit quite poorly. Finally, in model F, we switched schizoaffective disorder and other nonaffective psychoses. Like models C and D, the fit of this model was essentially indistinguishable from that of the a priori ordering.

DISCUSSION

Our results are consistent with the assumption of a single underlying familial vulnerability to the schizophrenia spectrum disorders. The pattern of aggregation and coaggregation of five psychiatric syndromes in relatives from the Roscommon Family Study is compatible with the hypothesis that these disorders are all manifestations of a single underlying liability that differ only in severity. Baron and Risch (11) reached a similar conclusion from their family study data, although they examined only three disorders: narrow schizophrenia, broad schizophrenia, and schizotypal personality disorder. Our results, however, are at variance with those reported by Tsuang et al. (12). Their study had three noteworthy methodological differences with the present report. First, they had only one group of index probands—those with schizophrenia. Second, they considered as part of the narrow schizophrenia spectrum several disorders that we did not consider, including phobia, obsessive-compulsive disorder, and antisocial and other personality disorders. Their broad definition of the schizophrenia spectrum included all anxiety disorders, depressive neurosis, and all personality disorders. Third, the interview on which their sample was based (35) had very limited information about schizophrenia spectrum personality traits.

Our results, if confirmed, have potentially significant implications for several areas of schizophrenia research. If familial aggregation is a useful guide to genetic effects, these findings would support the inclusion of a broad range of schizophrenia spectrum disorders in attempts to identify the chromosomal location of susceptibility genes for schizophrenia (36). In attempts to clarify the pathophysiological or neurophysiological basis of schizophrenia, our results suggest that the inclusion of subjects with nonschizophrenic psychoses or schizotypal personality disorder may be useful.

We estimated in the Roscommon Family Study that the correlation in liability to schizophrenia spectrum disorders between probands and first-degree relatives was 0.36. This figure can usefully be compared with correlations in liability to schizophrenia (with a 95% confidence interval) that can be calculated from the four most similar large family studies of schizophrenia (more than 200 assessed relatives of probands) completed and published since 1985 (10): mean=0.38, SD=0.06 (9), mean=0.37, SD=0.08 (14), mean=0.28, SD=0.08 (37), and mean=0.38, SD=0.06 (38). The mean of these four studies (0.35) is strikingly similar to that found in this report. In the only result that is directly comparable to our estimate, Baron and Risch calculated, by applying a multiple threshold model to their family data, the “transmissibility” of the schizophrenia spectrum (11). This figure, equal to twice the correlation in liability between probands and first-degree relatives, was estimated at 0.72 (SD=0.15).

If, as suggested by twin and adoption studies (39–41), most or all of the familial resemblance for schizophrenia and schizophrenia spectrum disorders is a result of genetic factors, then the correlation in liability observed among first-degree relatives should equal approximately half of the heritability (because first-degree relatives, on average, share half their genes in common). On the other hand, if shared environmental factors played a major role in the familial transmission of schizophrenia,
nia spectrum disorders, then the resemblance in first- 
degree relatives (especially siblings who share the same 
rearing environment) should substantially exceed that 
predicted from the heritability.

In a previous review of nine major twin studies of 
 schizophrenia (41), the weighted estimate of the herita-
bility of liability to schizophrenia was 0.68 (SD=0.04). 
Path analytic models based on aggregate results from 
twin and family studies (42) have produced similar re-
sults. If familial resemblance for schizophrenia is due 
only to additive genetic factors, these figures predict 
that the correlation in liability to schizophrenia (and 
associated spectrum conditions) between probands and 
first-degree relatives should be 0.34—similar to that 
observed. The convergence of these diverse and in-
dependent results is encouraging and consistent with 
the hypothesis that the schizophrenia spectrum is highly 
familial and that most of the familial aggregation of these 
disorders results from genetic factors.

While we found substantial evidence in favor of the 
 hypothesized schizophrenia spectrum, we were less suc-
cessful at definitively setting an order of severity for 
the diagnostic categories within this spectrum. Our results 
suggest that schizophrenia belongs at the most severe 
end of the spectrum and psychotic affective illness be-
longs at the milder end. Between these two extremes, 
our study provided little information about ordering. 
With respect to schizotypal/paranoid personality disor-
der, this lack of information is not surprising, since we 
ascertained only 53 relatives of probands with this dis-
order. Only very large sample studies are likely to have 
sufficient statistical power to definitively resolve the or-
der of severity for the disorders within the schizophre-
nia spectrum.

The results of this report should be interpreted in 
the context of four potential methodologic limitations. 
First, we have not considered all possible schizophre-
nia spectrum disorders. For example, the Roscommon 
Family Study provides some evidence that schizoid 
and avoidant personality disorder (16) and simple schizo-
phrenia (43) may also be part of the schizophrenia 
spectrum. However, these disorders are so uncommon 
that they could not be usefully included in the present 
analyses.

Second, these analyses focused solely on schizophre-
nia spectrum psychopathology. From this perspective, 
schizoaffective disorder and psychotic affective illness 
appear to belong in the schizophrenia spectrum. How-
ever, if affective illness in relatives is examined, a quite 
different picture emerges. Unlike the other disorders 
considered, relatives of probands with schizoaffective 
disorder and psychotic affective illness have a greater 
risk for affective illness (17). Thus, our construct of the 
schizophrenia spectrum does not imply that the condi-
tions on that spectrum do not differ in their liability to 
other psychiatric disorders.

Third, we tested only whether the distribution of dis-
orders in proband-relative pairs was consistent with 
that predicted by a multiple threshold model with a 
single liability to illness. This model fit very well and pro-
vided no indication that more complex models (e.g., 
models that incorporate two or more independent li-
bility dimensions) were necessary.

Finally, our multiple threshold model assumed that 
the vulnerability to schizophrenia spectrum disorders 
was multifactorial and due to at least a moderate num-
ber of distinct genetic and environmental effects of 
small to modest size (44, 45). If a large proportion of 
schizophrenia spectrum disorders were due to a single 
gene of large effect, then our parameter estimates may 
be incorrect. However, the available evidence does not 
favor this hypothesis (46).

REFERENCES

1. Bleuler E: Dementia Praecox or the Group of Schizophrenias (1908). Translated by Zinkin J. New York, International Univer-
sities Press, 1950

2. Katon WS, Rosenthal D, Wender PH, Schulzinger F: The types and 
prevalence of mental illness in the biological and adoptive fami-
lies of adopted schizophrenics. J Psychiatr Res 1968; 6:345-
362

3. Katon WS, Rosenthal D, Wender PH, Schulzinger F, Jacobsen B: 
The biological and adoptive families of adopted individuals 
who became schizophrenic: prevalence of mental illness and 
other characteristics, in The Nature of Schizophrenia: New 
Approaches to Research and Treatment. Edited by Wynne LC, 
Cromwell RL, Matthysse S. New York, John Wiley & Sons, 
1978

4. Kendler KS: Diagnostic approaches to schizotypal personality 
disorder: a historical perspective. Schizophr Bull 1985; 11:538-
553

5. Krahnen E: Dementia Praecox and Paraphrenia (1919). Trans-
lated by Barclay RM; edited by Robertson GM. New York, Rob-
ert E Krieger, 1971

6. Rudin E: Studien uber Vererbung und Entstehung geistiger Stor-
ungen, I: Zur vererbung und neuentstehung der Dementia praec-
ox (Studies on the inheritance and origin of mental illness, I: the 
problem of the inheritance and primary origin of dementia praec-
ox), in Monographien aus dem Gesamtbereich der Neurologie 

gustine, 1938

8. Kendler KS, Gruenberg AM: An independent analysis of the Co-
ophagen sample of the Danish Adoption Study of Schizophre-
nia, VI: the relationship between psychiatric disorders as defined 
by DSM-III in the relatives and adoptees. Arch Gen Psychiatry 
1984; 41:553-564

first-degree relatives of schizophrenic and surgical control pa-
patients: a family study using DSM-III criteria. Arch Gen Psychiatry 
1985; 42:770-779

10. Kendler KS, Diehl SR: The genetics of schizophrenia: a current, 
genetic-epidemiologic perspective. Schizophr Bull 1993; 19:261-
283

11. Baron M, Risch N: The spectrum concept of schizophrenia: evi-
dence for a genetic-environmental continuum. J Psychiatr Res 
1987; 21:257-267

12. Tsuang MT, Bacher KD, Fleming JA: A search for "schizophre-
nia spectrum disorders": an application of a multiple threshold 
model to blind family study data. Br J Psychiatry 1983; 143:572-
577

13. Kendler KS, McGuire M, Gruenberg AM, O'Hare A, Spellman 
M, Walsh D: The Roscommon Family Study, I: methods, diag-
nosis of probands and risk of schizophrenia in relatives. Arch 
Gen Psychiatry 1983; 50:527-540

study of schizophrenia and normal control probands: impli-
cations for the spectrum concept of schizophrenia. Am J Psychi-
atriy 1985; 142:447-455


23. Essén-Möller E: The calculation of morbidity risk in parents of index cases, as applied to a family sample of schizophrenics. Acta Genet 1955; 5:334-342


29. Neale MC: Statistical Modelling With Mx. Richmond, Virginia Commonwealth University, Medical College of Virginia, Department of Human Genetics, 1991


44. Falconer DS: The inheritance of liability to certain diseases, estimated from the incidence among relatives. Ann Hum Genet 1965; 29:51-76
