Personality Disorders Among the Relatives of Schizophrenia Patients

by Wolfgang Maier, Dirk Lichtermann, Jürgen Minges, and Reinhard Heun

Abstract

In light of current linkage studies in schizophrenia, research on the “schizophrenia spectrum” deserves increased attention for an exact determination of the affected phenotype: Those disorders that have a much higher prevalence among biological relatives of schizophrenia patients are supposed to share common etiological factors with “core” schizophrenia. However, there is controversy over which of the DSM-III-R personality disorders should be included in the spectrum. In a controlled family study of inpatients with a DSM-III-R diagnosis of schizophrenia (n = 101), schizophreniform and schizoaffective disorders (n = 69), and unipolar major depression (n = 160), familial rates of personality disorders were assessed through personal interviews and compared with prevalence rates in 109 control families from the community. As predicted, schizotypal personality disorder occurred more frequently in the nonpsychotic relatives of schizophrenia probands (2.1%) than in the families of unscreened controls (0.3%). Paranoid personality disorder was more frequent in relatives of probands with unipolar depression (2.9%) than in relatives of schizophrenia patients (1.7%), and controls revealed the lowest rate (0.9%). Schizoid personality disorder, however, was extremely rare in all sample groups (between 0.3% and 0.7%), providing no sufficient statistical power for detection of group differences. Further analysis of the DSM-III-R criterion symptoms of schizotypal personality disorder demonstrated that items describing “negative” symptomatology are the main source of familial aggregation, but “psychotic-like” personality features are also contributing factors.


A familial link between schizophrenia and peculiar patterns of personality and behavior, which do not fit the diagnostic requirements for schizophrenia, has been recognized since the early days of genetic research in psychiatry (Rüdin 1916). This relationship has been rediscovered by recent adoption studies (Kety et al. 1968; Kety 1988) and has subsequently attracted a lot of attention mainly because of its implications for phenotype identification in linkage studies. The familial relationship between core schizophrenia and other nonschizophrenic disorders (e.g., particular personality disorders) suggests that the phenotypic boundaries for linkage studies should be extended beyond the core cases of schizophrenia; a broader definition of affection status could increase the sensitivity of identification of the affected phenotype without substantially enhancing the rate of “false” positives. The validity of this procedure is also corroborated by the finding that the relationship between schizophrenia and certain personality disorders (Kendler 1988) is genetic in origin.

This notion of the schizophrenia spectrum intends to combine those psychopathologically defined conditions that share etiological factors.

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with schizophrenia and therefore reflect an alternative expression of schizophrenia. Family studies have been instrumental in establishing this relationship. A familial relationship to core schizophrenia as seen in genetic studies is a necessary but insufficient criterion for components of the schizophrenia spectrum. There should be further evidence that the familial relationship is due to sharing of common risk factors. To date, schizoaffective disorders and particular personality disorders (Kendler et al. 1981; Kendler and Gruenberg 1984; Baron et al. 1985; Kendler 1988) have been considered as possible components of the schizophrenia spectrum. Although evidence for a strong familial link of schizoidia to schizoaffective disorders is well established (Kendler 1988), the strength of a familial link to personality disorders is less clear.

Schizotypal personality disorder and paranoid personality disorder (and in some family studies the two personality disorders combined) have been suggested as candidates of the schizophrenia spectrum (Stephens et al. 1975; Kendler and Gruenberg 1982; Kendler and Gruenberg 1984; Tregerman 1985). Schizoid personality disorder also shares psychopathological features with schizophrenia, but there is little evidence that this personality disorder is a component of the schizophrenia spectrum (Levinson and Mowry 1991). Although these hypotheses have been supported by adoption and family studies, they require reconsideration for the following reasons:

1. Verification of the familial link between schizotypal personality disorder and schizophrenia is needed because recent studies failed to find higher rates of schizotypal personality disorders among relatives of schizophrenia patients (Coryell and Zimmerman 1989; Squires-Wheeler et al. 1989).

2. Whereas a strong familial link between schizotypal personality disorder and schizophrenia has been supported by past family and adoption studies, the relationship between schizotypal and paranoid personality disorder (Stephens et al. 1975; Kendler and Gruenberg 1982; Kendler et al. 1984, 1985; Baron et al. 1985; Frangos et al. 1985; Coryell and Zimmerman 1989) seems to be weaker. Some of these studies supporting a familial link between paranoid personality disorder and schizophrenia have been criticized for overestimating this particular personality disorder (Rogers and Winokur 1988); therefore, further study of the relatedness between paranoid personality disorder and schizophrenia is needed.

3. Early investigations in families (Kretschmer 1921/1977) reported "schizoidia," a personality pattern characterized by oddness of behavior and lack of emotional reactivity, to be especially frequent among relatives of schizophrenia patients. The personality pattern of schizoidia includes the diagnostic criteria of schizotypal as well as schizoid personality disorder according to DSM-III-R (American Psychiatric Association 1987). Family studies in schizophrenia rarely examined the familial prevalence of schizoid disorder, except for Baron et al. (1985) and Coryell and Zimmerman (1989). These studies found an enhancement of rates in relatives of schizophrenia patients, which failed to be significant.

4. It has not been sufficiently tested to determine whether other personality disorders that do not belong to the "odd" personality disorder cluster are components of the schizophrenia spectrum. This failure might be especially relevant for avoidant personality disorder: Kretschmer (1921/1977) described the schizoid temperament (schizoidia) as an attenuated form of schizophrenia and also characterized this trait by hypersensitivity and avoidant behavior. Not only schizoid personality disorder but also the DSM-III-R category avoidant personality disorder reveals conceptual similarities with Kretschmer's concept of schizoidia; thus, its hypothetic relationship to the schizophrenia spectrum should be examined.

5. The relationship between schizotypal personality disorder and affective disorders needs clarification, since some family studies reported this relationship to be as strong as or even stronger than that between schizotypal personality disorder and schizophrenia (Schulz et al. 1986; Squires-Wheeler et al. 1989).

6. The current DSM-III-R definition of schizotypal personality disorder does not seem to be the most appropriate for the identification of deviant behavioral patterns in relatives of schizophrenia patients. Mainly, the so-called negative symptoms of social withdrawal and reduced functioning were postulated to be more sensitive than the positive symptoms of odd behavior and paranoid tendencies for the identification of relatives of schizophrenia probands (Gunderson et al. 1983).

These points will be discussed by presenting the relative frequency of personality disorders in the families of schizophrenia probands, of probands with affective...
disorders, and of unscreened matched control subjects recruited from the general population.

Methods

Recruitment and Diagnostic Assessments. We reported on a subsample of a comprehensive family study (Maier et al. 1993). Probands of this study were selected from 725 consecutively admitted inpatients who were not suffering from dementia. They were also required to have at least one living first-degree relative who was willing to be directly interviewed. Probands were interviewed with the Schedule for Affective Disorders and Schizophrenia—Lifetime Version for Axis-I disorders (SADS–LA; Mannuzza et al. 1986) and with the Structured Clinical Interview for DSM–III–R Personality Disorders (SCID–II; Spitzer et al. 1986). If they fulfilled the research diagnostic criteria of SCID–II or DSM–III–R criteria for either schizophrenia, schizophreniform or schizoaffective disorder, major mood disorder, alcoholism, or panic disorder (n = 625), all available first-degree relatives were interviewed using the same instruments.

There were 109 control probands (with at least one first-degree relative available for direct interview) recruited from the general population by a marketing company. The controls were matched by sex, age, educational and social levels, and residential area to a subsample of 109 randomly selected probands from the inpatient sample. Beyond these stratification criteria, the control sample was representative of the general population. It is especially noteworthy that this sample population was not pre-selected by psychiatric or medical diagnoses. Of the controls, 29 suffered from an Axis-I disorder (DSM–III–R) and 12 were diagnosed with an Axis-II disorder (6 with an additional Axis-I lifetime diagnosis). All probands and at least 80 percent of first-degree relatives in both comparison groups were directly interviewed with the SADS–LA and the SCID–II. First-degree relatives were also asked for a lifetime family history, except the probands, of major psychiatric disorders and bizarre and acting-out personality disorders in all relatives who were included in this study (with the exception of the proband). Family history information on other first-degree relatives of the proband was obtained in both samples from directly interviewed relatives of probands (including information on those relatives who were either dead or unavailable for direct interview). Telephone interviews were not conducted. Physicians making final diagnostic decisions on relatives were unaware of the status and diagnosis of the index case and vice versa. The relatives’ interviews and any other diagnostic assessment were performed keeping raters as blind as possible to the index probands’ diagnostic status. Despite these limitations an observational bias, which results in falsely positive enhancement of familial risk of suspected schizophrenia spectrum disorders, or an artificially increased intrafamilial diagnostic homogeneity was unlikely to occur. Measures to prevent bias were taken, such as selecting interviewers who were well-trained clinical assistants with at least 4 years of medical school and 3 months of clinical training in psychiatry. The interviewers’ initial training comprised 20 sessions with final reliability testing, which was repeated in 6-month intervals during the study. Test-retest reliability measures for major Axis-I disorders and for personality disorders were 0.70 (kappa) or higher for all diagnoses relevant in this report.

Best estimate diagnoses were established by two experienced psychiatrists. When they did not concur, a third psychiatrist was asked to make the final decision. As suggested by Leckman et al. (1982) all subjects received an ultimate Axis-I diagnosis by a clinician’s (blind to the particular familial relationship between subjects) review of interview results, case records for inpatients, and family history. Best estimate Axis-II diagnoses were obtained by using the SCID–II. Final diagnoses of subjects also were based on family history and medical records, whereas diagnoses of the presence or absence of personality disorders had to rely nearly exclusively on the SCID–II interview data.

In order to base diagnostic assessments of personality disorder on a sufficiently long temporal interval, only patients older than 20 were considered. A criterion was established for personality disorders to have initially occurred between the ages of 18 and 30 and to have been present during most of their adulthood. It was further required that an Axis-II diagnostic criterion would not result from a lack of remission or only partial remission of an Axis-I disorder. Consequently, personality deviations in subjects with chronic schizophrenia, schizoaffective, affective, or severe anxiety disorders were only considered as present if they were not consequences of an Axis-I disorder. The relationship between different personality
disorders was modeled in a hierarchy-free manner (e.g., if a subject fulfilled criteria for two personality disorders, both were regarded as present).

Selection of Comparison Groups. To examine the potential relationship of personality disorders to the schizophrenia spectrum, four comparison groups were extracted from the total sample of families of probands and controls.

1. The crucial test to determine whether a diagnostic group belongs to the schizophrenia spectrum is a higher prevalence rate of this particular diagnosis in families of probands with core schizophrenia. According to the DSM-III-R, the presence of severe positive symptoms at one time, the absence of prominent affective symptoms over a longer period of time, and long-term schizophrenic symptoms represent the components of core schizophrenia.

2. Schizoaffective and schizoaffective disorders, depressed type (DSM-III-R) are also likely to belong to the schizophrenia spectrum. In this case, other spectrum disorders should be related to schizoaffective and schizoaffective disorders in a similar manner because they are related to core schizophrenia. Consequently, probands with schizoaffective disorder (unipolar depressive type) or schizoaffective disorder (DSM-III-R) were combined as a second comparison group ("other psychotic disorders"). The comparison of familial rates of assumed spectrum disorders between this group and the control group facilitates testing the consistency of the schizophrenia spectrum. Probands with bipolar affective disorder were not included in this group because this disorder is also linked to bipolar affective disorder, which has a divergent pattern of associated personality variations (Levinson and Levitt 1987; Maier et al. 1992b).

This subgroup of patients is heterogeneous: Some patients diagnosed with schizophreniform disorder may develop chronic schizophrenia in the followup, whereas others may have a complete remission after 6 months; some patients with schizoaffective disorder may develop chronic impairment, whereas others might present with either a short, single episode or recurrent episodes with intermediate and subsequent complete remission. Although it would be possible to subdivide the whole group by manifest chronicity, the remaining subgroup of nonchronic patients would again be heterogeneous as determined by the future course of their disorder. Because of these circumstances and the low number of patients in the various subgroups, we avoided further subdivisions.

3. For examining the diagnostic specificity of schizophrenia spectrum, a further comparison group consisting of probands with unipolar major depression without psychotic features (DSM-III-R) was introduced.

4. Control families may either be identified by control probands defined by absence of psychiatric disorders or by probands recruited from the general population in a representative manner irrespective of their diagnostic status. Tsuang et al. (1988) and Kendler (1988) argued that the "true" prevalence rates of disorders are underestimated in control families if only healthy control probands are considered; false significant findings might, therefore, result if families of patients are compared with families of healthy controls. Therefore, the control sample used in this report also included those who received a psychiatric lifetime diagnosis (Maier et al. 1993).

The primary focus of this report was on the extent to which personality disorders might contribute to the schizophrenia spectrum. Prevalence rates of personality disorders were compared between first-degree relatives of proband groups to characterize this relationship. However, there might be symptomatic overlap between the well-established spectrum disorders—schizophrenia, schizoaffective, and schizophreniform disorders—and particular personality disorders. An observed familial link between schizophrenia and a particular personality disorder might therefore be the consequence of similarities in diagnostic criteria but not necessarily due to a true familial relationship. To avoid this potential source of error, all relatives with a DSM-III-R diagnosis of either schizophrenia, schizophreniform, or schizoaffective disorder were excluded from further analyses in all comparison groups. The following data in table 1 refer exclusively to directly interviewed relatives. Only those relatives with the suspected spectrum personality disorders who were not comorbid for schizophrenia were included in the evaluation.

Statistical Methods. Statistical analysis of this study was complicated by the multiplicity of tests, limitations of sample size, and the relatively low statistical power to detect differences. Therefore, we only considered the comparison between schizophrenia probands and controls with regard to the prevalence of schizotypal person-
Table 1. Sample sizes and sociodemographic characteristics

<table>
<thead>
<tr>
<th>Proband groups by DSM-III-R</th>
<th>Schizophrenia</th>
<th>Schizophreniform or schizoaffective disorder (depressed)</th>
<th>Unipolar major depression (nonpsychotic)</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Probands</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number</td>
<td>101</td>
<td>69</td>
<td>160</td>
<td>109</td>
</tr>
<tr>
<td>Age (mean)</td>
<td>36.8</td>
<td>36.8</td>
<td>47.2</td>
<td>38.9</td>
</tr>
<tr>
<td>Gender (male, %)</td>
<td>59.4</td>
<td>49.3</td>
<td>40.6</td>
<td>51.4</td>
</tr>
<tr>
<td>Number of relatives</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>382</td>
<td>264</td>
<td>602</td>
<td>419</td>
</tr>
<tr>
<td>Living</td>
<td>344</td>
<td>235</td>
<td>532</td>
<td>378</td>
</tr>
<tr>
<td>Interviewed</td>
<td>289</td>
<td>198</td>
<td>450</td>
<td>320</td>
</tr>
<tr>
<td>Interviewed relatives</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (mean)</td>
<td>44.8</td>
<td>45.0</td>
<td>46.0</td>
<td>40.2</td>
</tr>
<tr>
<td>Gender (male, %)</td>
<td>48.4</td>
<td>48.0</td>
<td>49.6</td>
<td>47.2</td>
</tr>
</tbody>
</table>

Note.—DSM-III-R = Diagnostic and Statistical Manual of Mental Disorders—Revised (American Psychiatric Association 1987).

Prevalence rates of personality disorders in the total control sample, the overall prevalence rate of personality disorders was 10.3 percent (10.5% in females and 9.9% in males). The most frequently occurring personality disorders were obsessive-compulsive (2.2%), passive-aggressive (1.9%), and dependent (1.6%). Schizotypal, schizoid, and paranoid personality disorders were rare in the control sample: 0.3 percent, 0.3 percent, and 0.9 percent, respectively. Further details of prevalence in a general population sample are presented in Maier et al. (1992a).

Relatives of Schizophrenia Probands Compared With Controls. Of the 11 DSM-III-R personality disorders, only schizotypal personality disorder was significantly (p = 0.05) more frequent among the relatives of schizophrenia probands compared with relatives of controls: The relative frequency of schizotypal personality disorder in schizophrenia probands' families (2.1%) was sevenfold higher than in the families of controls (table 2).
### Table 2. Prevalence of personality disorders (DSM-III-R) in proband groups' first-degree relatives

<table>
<thead>
<tr>
<th>Relatives by proband groups</th>
<th>Schizophreniform or schizoaffective</th>
<th>Unipolar major depression</th>
<th>Controls</th>
<th>Global</th>
<th>SZ vs. C</th>
<th>SF/SA vs. C</th>
<th>DEP vs. C</th>
<th>SZ vs. DEP</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cluster A</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paranoid</td>
<td>5 (1.7%)</td>
<td>4 (2.0%)</td>
<td>13 (2.9%)</td>
<td>3 (0.9%)</td>
<td>3.4</td>
<td>0.7</td>
<td>1.0</td>
<td>3.8</td>
</tr>
<tr>
<td>Schizoid</td>
<td>2 (0.7%)</td>
<td>1 (0.5%)</td>
<td>2 (0.4%)</td>
<td>1 (0.3%)</td>
<td>0.5</td>
<td>0.5</td>
<td>0.1</td>
<td>0.1</td>
</tr>
<tr>
<td>Schizotypal</td>
<td>6 (2.1%)</td>
<td>4 (2.0%)</td>
<td>3 (0.7%)</td>
<td>1 (0.3%)</td>
<td>6.9</td>
<td>4.5</td>
<td>3.8</td>
<td>0.5</td>
</tr>
<tr>
<td><strong>Cluster B</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Antisocial</td>
<td>0</td>
<td>1 (0.5%)</td>
<td>1 (0.2%)</td>
<td>1 (0.3%)</td>
<td>1.9</td>
<td>1.3</td>
<td>0.1</td>
<td>0.5</td>
</tr>
<tr>
<td>Borderline</td>
<td>3 (1.0%)</td>
<td>2 (1.0%)</td>
<td>9 (2.0%)</td>
<td>4 (1.3%)</td>
<td>1.6</td>
<td>0.1</td>
<td>0.1</td>
<td>0.7</td>
</tr>
<tr>
<td>Histrionic</td>
<td>3 (1.0%)</td>
<td>4 (2.0%)</td>
<td>7 (1.6%)</td>
<td>4 (1.3%)</td>
<td>0.9</td>
<td>0.1</td>
<td>0.5</td>
<td>0.1</td>
</tr>
<tr>
<td>Narcissistic</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td><strong>Cluster C</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Avoidant</td>
<td>5 (1.7%)</td>
<td>4 (2.0%)</td>
<td>9 (2.0%)</td>
<td>4 (1.3%)</td>
<td>0.8</td>
<td>0.2</td>
<td>0.5</td>
<td>0.7</td>
</tr>
<tr>
<td>Dependent</td>
<td>4 (1.4%)</td>
<td>4 (2.0%)</td>
<td>8 (1.8%)</td>
<td>5 (1.6%)</td>
<td>0.3</td>
<td>0.4</td>
<td>0.1</td>
<td>0.1</td>
</tr>
<tr>
<td>Obsessive-Compulsive</td>
<td>8 (2.8%)</td>
<td>9 (4.5%)</td>
<td>14 (3.1%)</td>
<td>7 (2.2%)</td>
<td>2.2</td>
<td>0.2</td>
<td>2.2</td>
<td>0.6</td>
</tr>
<tr>
<td>Passive-Aggressive</td>
<td>3 (1.0%)</td>
<td>3 (1.5%)</td>
<td>8 (1.8%)</td>
<td>6 (1.9%)</td>
<td>0.9</td>
<td>0.7</td>
<td>0.1</td>
<td>0.0</td>
</tr>
</tbody>
</table>

**Note.**—DSM-III-R = Diagnostic and Statistical Manual of Mental Disorders—Revised (American Psychiatric Association 1987); SZ = schizophrenia; SF/SA = schizoaffective; DEP = unipolar major depression; C = controls.

1°df = 3, global; df = 1, proband groups.

2°mean = 0.025, p < 0.05.

The comparison of the prevalence of schizoid and schizotypal personality disorders was selected for each domain testing (p = 0.025 for each hypothesis). The incidence of the personality disorders was not significantly higher in proband families compared to control families; the presence of schizotypal personality disorder (1.0% vs. 1.3%) and for schizoid personality disorder (1.0% vs. 1.3%), and for schizoid personality disorder (1.0% vs. 1.3%).
families. The rate of schizotypal personality disorder was nearly equal in families of probands with schizophrenia (2.1%) and families of other psychotic disorder probands (2.0%). However, the differences of familial rates between probands with other psychotic disorders and controls were nonsignificant because of lower sample size.

Prevalence in Families of Probands With Unipolar Depression Compared With Families of Schizophrenia Probands. It is especially noteworthy that paranoid personality disorder was more frequent in families of probands with unipolar depression (2.9%) than in families of schizophrenia probands (1.7%) or of probands with either schizophreniform or schizoaffective disorder, depressed type (2.0%). The familial rates for borderline personality disorder in probands with unipolar depression (2.0%) also were slightly higher than in schizophrenia probands (1.0%) or in probands with a diagnosis of other psychotic disorders (1.0%). Schizotypal personality disorder, however, was consistently more frequent in the families of schizophrenia probands than in control families or in the families of depressive probands (2.1% in schizophrenia families and 2.0% among relatives of other psychotic disorder probands vs. 0.7% among depressive probands' families and 0.3% in control families). The familial rates of schizotypal personality disorder in probands with schizophrenia and in probands with unipolar depression differed significantly (p < 0.05). The prevalence of schizoid personality disorder was very low among all comparison groups (< 1.0%) and was slightly but not significantly higher in relatives of schizophrenia probands (0.7%).

Definition of Schizotypal Personality Disorder. Schizotypal personality disorder was more common in schizophrenia families compared with controls recruited from the general population and yet, to a lesser degree, in comparison with probands with unipolar major depression. Since the diagnosis of schizotypal personality disorder is based on nine criterion symptoms, the next step was to clarify the relative contribution of particular items of the schizotypal personality disorder category discriminative of this diagnostic category.

Multiple testing was controlled by adjusting the error rate for individual items according to Bonferroni. Four of the nine items revealed a trend (p = 0.10, global; p = 0.0011, individual items) for discrimination between relatives of schizophrenia probands and controls (table 3): “no close friends or confidants” (item 6); “odd speech” (item 7); “inappropriate or constricted affect” (item 8); “odd behavior” (item 5). Only three criteria distinguished between the families of schizophrenia patients and the families of probands with unipolar major depression: “odd, eccentric, or peculiar behavior or appearance” (item 5), “odd speech” (item 7), and “inappropriate or constricted affect” (item 8). All three of these characterize the relatives’ expressive behavior.

Discussion

Scope of the Schizophrenia Spectrum. This study supports the hypothesis of a schizophrenia spectrum with the position that there is a familial link between schizophrenia and deviant personality patterns: The prevalence of schizotypal personality disorder (DSM-III-R) was higher in families of schizophrenia probands. However, the sevenfold higher prevalence rate in relatives of schizophrenia patients shortly failed the a priori fixed alpha error for confirmatory testing (p = 0.025) due to the limited power to detect differences between sample groups. Although the absolute rates vary widely between different studies, a high prevalence rate of schizotypal personality disorder in families of schizophrenia probands agrees with findings of the Danish adoption study and the family studies by Baron et al. (1985), Kendler et
Table 3. Prevalence of individual criteria for schizotypal personality disorders in proband groups' first-degree relatives

<table>
<thead>
<tr>
<th>Criteria (DSM-III-R)</th>
<th>Proband groups</th>
<th>Statistical comparisons (chi-square)¹</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SZ (n = 289)</td>
<td>DEP (non-psychotic) (n = 450)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(1) Ideas of reference</td>
<td>12 (4.2%)</td>
<td>13 (2.9%)</td>
</tr>
<tr>
<td>(2) Excessive social anxiety</td>
<td>20 (6.9%)</td>
<td>33 (7.3%)</td>
</tr>
<tr>
<td>(3) Odd beliefs or magical thinking</td>
<td>15 (5.2%)</td>
<td>25 (5.6%)</td>
</tr>
<tr>
<td>(4) Unusual perceptual experiences</td>
<td>13 (4.5%)</td>
<td>14 (3.1%)</td>
</tr>
<tr>
<td>(5) Odd, eccentric, or peculiar</td>
<td>15 (5.2%)</td>
<td>4 (0.9%)</td>
</tr>
<tr>
<td>behavior or appearance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(6) No close friends or confidants</td>
<td>57 (19.7%)</td>
<td>69 (15.3%)</td>
</tr>
<tr>
<td>(7) Odd speech</td>
<td>18 (6.2%)</td>
<td>9 (2%)</td>
</tr>
<tr>
<td>(8) Inappropriate or constricted</td>
<td>20 (6.9%)</td>
<td>13 (2.9%)</td>
</tr>
<tr>
<td>affect</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(9) Suspiciousness or paranoid</td>
<td>21 (7.3%)</td>
<td>33 (7.3%)</td>
</tr>
</tbody>
</table>

Note.—DSM-III-R = Diagnostic and Statistical Manual of Mental Disorders—Revised (American Psychiatric Association 1987); SZ = schizophrenia; DEP = unipolar major depression; C = controls

¹df = 3, global; df = 1, proband groups.
²mean = 0.0056, p < 0.05.
³p < 0.0011.
⁴mean = 0.0011, p < 0.0056.
al. (1984), and Frangos et al. (1985). The relationship of schizotypal personality disorder to those Axis-I disorders presumed to belong to the schizophrenia spectrum is consistent because the prevalence of schizotypal personality disorder was also increased in families of probands with schizoaffective, delusional, or schizoaffective disorders (DSM-III-R). These findings, however, contradict data obtained by Coryell and Zimmerman (1989) (2% in families of schizophrenia probands and 5% in families of the Research Diagnostic Criteria [RDC; Spitzer et al. 1978] schizoaffective probands). The discrepancy with the latter might be explained by the frequent use of telephone interviews in that study, a method that is likely to be less accurate in the assessment of items referring to expressive behavior. Other studies comparing the familial prevalence of schizotypal personality disorder between these two proband groups are unavailable.

The schizophrenia spectrum concept claims a specific relationship of the spectrum disorders to schizophrenia. Since diagnostic specificity is implicit in this statement, schizophrenia spectrum disorders should not be related to affective disorders as they are to schizophrenia. Schizotypal personality disorder matched this requirement. Its prevalence in families of probands with unipolar depression was lower than in families of schizophrenia probands and not significantly higher compared with control families. Paranoid personality disorder did not reveal a strong tendency to aggregate in families of schizophrenia probands as previously reported by Baron et al. (1985) and the Danish adoption study (Kendler and Gruenberg 1982), but this was not replicated by others (Kendler et al. 1984, 1985; Frangos et al. 1985; Coryell and Zimmerman 1989). Our study revealed a particular familial relatedness of paranoid personality disorder to affective disorder (unipolar depression was more strongly related to paranoid personality disorder than schizophrenia). While this relationship was not observed by Coryell and Zimmerman (1989), it is partly supported by the New York High-Risk Study. Squires-Wheeler et al. (1989) reported a higher rate of suspiciousness in families of probands with affective disorders than in families of schizophrenia probands. One possible explanation for the discrepancy between studies with respect to the relationship between paranoid personality disorder and schizophrenia has been proposed by Rogers and Winokur (1988): Delusional disorder (paranoia) is likely to be considered as schizophrenia by the RDC, and there is empirical evidence that delusional disorder is not genetically related to schizophrenia but seems to be related to paranoid personality traits. Accordingly, we found no link between paranoid personality disorder and schizophrenia when we used DSM-III-R criteria, which strictly separate schizophrenia and schizoaffective disorder from delusional disorder.

The prevalence rates of schizotypal and paranoid personality disorders are low in our study compared with those of the Danish Adoption Study (Kendler and Gruenberg 1984) and the study by Baron et al. (1985) who reported prevalence rates of schizotypal and of paranoid personality disorder of 14.6 and 7.3 percent, respectively, in relatives of schizophrenia probands and of 2.1 and 2.7 percent, respectively, in control families. Several more recent family studies yielded lower mean overall rates (e.g., the Iowa Study [Coryell and Zimmerman 1989]; the New York High-Risk Study [Squires-Wheeler et al. 1989]; the family studies by Kendler [1988] and by Frangos et al. [1985]). Although the two studies with relatively high prevalence rates reported significantly increased rates in families of schizophrenia probands, the remaining studies were not in agreement on this point. Several explanations for the divergent results are possible. There is a tendency across these studies for the rates of schizotypal personality disorder to be higher both in relatives of schizophrenia probands and of controls in studies where more focused instruments are used rather than those instruments that cover the entire personality disorder spectrum. Instruments focusing on only a few personality disorders comprise more detailed questions per diagnostic criterion and thus have a higher sensitivity than the less focused generic instruments. The difference between the rates of Baron et al. (1985) and other American studies (e.g., Squires-Wheeler et al. 1989) and our study can be explained by insufficient specification of diagnostic criteria for Axis-II disorders. As a result, the intercenter reliability might be low for particular criteria, which may lead to different thresholds for matching a criterion. Since no anchor points are proposed by the diagnostic manuals, different studies may use different thresholds for matching a criterion. There is a striking similarity, however, be-
tween the research of Baron et al. (1985) and our study with respect to prevalence rates of schizotypal and schizoid personality disorders (e.g., affective constriction and social isolation), it might be expected that schizoid personality disorder aggregates among relatives of schizophrenia probands. Further aggregation might be seen, since two criteria that differentiated relatives of schizophrenia probands from relatives of controls in the present study are also criteria for schizoid personality disorder. As expected, schizoid personality disorder was more frequent in families of schizophrenia probands than in families of controls, but not significantly so (partly because of the low base rate of schizoid personality disorder). The family studies by Baron et al. (1985) and Frangos et al. (1985) reported a similar nonsignificant relationship. A less stringent definition of schizoid personality disorder (e.g., requiring less than five criteria for the disorder to be present) might establish a clear and positive familial relationship between schizophrenia and this redefined disorder and thus reconcile recent empirical work with the classical concepts of Kretschmer (1921/1977) and Kallmann (1938).

According to studies by Coryell and Zimmerman (1989), Baron et al. (1985), and Frangos et al. (1985), personality disorders that were not part of the odd personality disorder cluster were unlikely to belong to the schizophrenia spectrum. This statement especially applies to avoidant and borderline personality disorders. A reanalysis of the Danish Adoption Study found borderline personality disorder to be more frequent in biological relatives of schizophrenia probands, but this resulted mainly from an overlap of schizotypal and borderline personality disorder in this sample (Gunderson et al. 1985). All subsequent family studies (including our study) were not able to replicate a high frequency of co-occurring schizotypal and borderline personality disorders or an aggregation of borderline personality disorder alone in biological relatives of schizophrenia probands.

In family studies, the view of schizotypal personality disorder as a less severe variant of schizophrenia would lead researchers to predict that the familial rates of schizotypal personality disorder are higher in proband groups at increased risk for schizophrenia. If the schizophrenia spectrum concept is consistent, it can be expected that the schizotypal personality disorder (or at least some of its symptomatic components) will also aggregate in families of probands with other disorders belonging to the spectrum such as schizoaffective and schizophreniform disorders. The present study also corroborated this prediction.

Proposals for a Redefinition of Schizotypal Personality Disorder. Both the "negative" and the majority of "positive" symptoms (exceptions: odd beliefs or magical thinking, suspiciousness) were at least twice as common in families of schizophrenia patients than in the control sample. The only study comparing the frequency of particular items of schizotypal personality disorder between families of probands with schizophrenia and families of probands with affective disorders, as well as families of control probands, was derived from the New York High-Risk Study (Squires-Wheeler et al. 1989). Although the absolute prevalence rates of criteria are at variance between the two studies, the same conclusions for all schizotypal personality disorder criteria were obtained with two exceptions: "social isolation" and "undue social anxiety" were nearly as common among control families as in families of schizophrenia patients in the New York sample. Both criteria were substantially more frequently fulfilled in families of schizophrenia patients according to our data. There is partial agreement with the New York sample when diagnostic specificity is taken into account. We found three criteria describing expressive behavior ("odd speech," "inappropriate affect," "odd behavior") to distinguish families of schizophrenia probands from families of controls but not families of probands with unipolar depression from control families, whereas Squires-Wheeler et al. (1989) found two criteria ("odd behavior" and "recurrent illusions") to fulfill both conditions.
Kendler (1985), considered affective flattening and bizarre behavior as the most prominent features in this respect. On the basis of these reports (primarily Kretschmer 1921/1977; and Kallmann 1938), we also expected social isolation to be a specific feature of personality disorders belonging to the schizophrenia spectrum, but this sign was nearly as common in relatives of affective disorder probands both in our study and in the New York High-Risk Study. A reanalysis of the Danish Adoption Study (Gunderson et al. 1983) also placed emphasis on negative symptoms of schizotypal personality disorder and stressed especially the symptoms of affective flattening and of social withdrawal and anxiety. However, the focus of this reanalysis was placed on the differentiation between schizophrenia and control families and not on the diagnostic specificity of this group difference.

All of these studies, however, including this one, might have overreported the extent of deviancy in those features most readily observed (e.g., odd speech, bizarre appearance or behavior), regardless of the degree of cooperativeness shown during the diagnostic interview. All available evidence suggests that the sensitivity of the identification of relatives is higher for the negative symptoms of schizotypal personality disorder. If diagnostic specificity (vs. affective disorder) of the relationship to schizophrenia is considered a crucial criterion, mainly deviant patterns of expressive behavior (affective flattening, odd behavior) will provide the most appropriate criteria. Thus, the current DSM–III–R definition of schizotypal personality disorder is not in complete agreement with family investigations. Positive symptoms are more common among treated cases than among family members affected with schizotypal personality disorder (Frances 1985). In contrast, negative symptoms may be relatively frequently found in high-risk subjects even in absence of a lifetime history of positive symptoms (subjects are apparently less likely to ask for medical care). The development of two lists of definitions for the same disorder, one for clinical and one for genetic studies, might therefore be an appropriate solution to this ambiguity.

Conclusion

This study replicated previous reports on a familial relationship between core schizophrenia and schizotypal personality disorder (Levinson and Mowry 1991), but it failed to establish a strong familial relationship between core schizophrenia and paranoid, schizoid, and other personality disorders that are not a part of the odd personality disorder cluster. It might be argued that this resulted in a narrow definition of the schizophrenia spectrum. Although this is currently the largest published study on the familial relationship between schizophrenia and personality disorders using modern diagnostic criteria, direct interviews, and blind testing, there was still a substantial limitation in detecting chi-squares for disorders with low prevalence rates. In view of the observed prevalence rates, a two- to threefold increase in sample size would be necessary to detect the significant difference of a two-fold increased risk.

A possible alternative view on schizotypal personality disorder is motivated by classical European psychiatry (Kety 1985). Schizotypal personality disorder as defined by DSM–III–R or in an improved definition might reflect a variant of schizophrenia (not a personality disorder) that does not meet the Schneiderian first-rank symptoms on which most of the diagnostic definitions of schizophrenia criteria (including DSM–III–R and RDC) are based. On the other hand, this hypothetical variant of schizophrenia shares a number of other features, which are often summarized under negative symptoms (e.g., deteriorated social and communicative behavior, affective flattening) with core schizophrenia. The specific focus on negative symptoms is validated by the familiarity of the features observed in this report. Bleuler recognized a non-Schneiderian subtype of schizophrenia, which was termed as latent schizophrenia or schizophrenia simplex (Kendler 1985). A major characteristic of this variant is the chronicity of the features and the limited social impairment. The relevance of this less restrictive concept of schizophrenia is underscored by the questionable validity of Schneiderian symptoms (McGuffin et al. 1984) in contrast to the established validity of negative symptoms (Lowing et al. 1983).

It is noteworthy that the International Classification of Diseases ICD–10 (World Health Organization 1991) recognizes the fundamental importance of personality-like negative symptom patterns by redefining Bleuler’s concept of schizophrenia simplex, which does not include any positive symptoms among the defining criteria. This diagnostic category is not consid-
Tsitourides, S.; Katsanou, N.; and of schizophrenia is assumed. Rather, a strong nosological relationship to the other variants of schizophrenia is assumed.

References


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