

Canadian Institutes of Health Research Instituts de recherche en santé du Canada

Submitted by CIHR Déposé par les IRSC

JPsychiatr Res. Author manuscript; available in PMC 2011 August 24.

Published in final edited form as: J Psychiatr Res. 1989 ; 23(3-4): 229–239.

DSM-III-R SCHIZOTYPAL PERSONALITY TRAITS IN OFFSPRING OF SCHIZOPHRENIC DISORDER, AFFECTIVE DISORDER, AND NORMAL CONTROL PARENTS

Elizabeth Squires-Wheeler, Andrew E. Skodol, Anne Bassett, and L. Erlenmeyer-Kimling New York State Psychiatric Institute and Columbia University, 722 West 168th Street, New York 10032, U.S.A

Summary

The aggregation of disorder in families identified by a schizophrenic disorder proband (index case) has provided indirect clues to the question of diagnostic boundaries of schizophrenic spectrum categories. The Danish Adoption Studies provided quasi-experimental evidence for the range of expression of a putative schizophrenic spectrum disorder which was subsequently denoted schizotypal personality disorder (STPD) in DSM-III-R. It has been hypothesized that such schizophrenic spectrum categories bear a genetic relationship to schizophrenic disorder and thus are continuous with schizophrenia in terms of etiology and pathogenesis. For meaningful use of such spectrum categories in genetic analyses, e.g., linkage analysis, it is important that rates of spectrum traits and disorder in normal control and in psychiatric control populations are known. The rate of DSM-III-R schizotypal traits and disorder was assessed in three offspring groups (ages 18–29) defined by parental diagnoses, including schizophrenic disorder (N= 90), affective disorder (N = 79), and no parental disorder (N = 161). The assessment was conducted by trained social workers and psychologists by means of a direct interview (Personality Disorder Examination). The interviewers were blind to the parental status and to previous psychiatric assessments of these offspring. The rates of three, four and five schizotypal features were elevated in the offspring with parental psychiatric disorder in contrast to the offspring with no parental psychiatric disorder. However, the rates between the offspring of the schizophrenic disorder parental group and the offspring of the affective disorder parental group did not differ significantly, thus failing to support the assumption of diagnostic specificity.

INTRODUCTION

Investigators have sought the diagnostic boundaries of a schizophrenic-spectrum disorder since the introduction of the nuclear syndrome of schizophrenia in 1911 (Bleuler, 1911Bleuler, 1950; Essen-Moller, 1946; Rado, 1960; Meehl, 1962; Heston, 1970; Shields, Heston & Gottesman, 1975). The aggregation of disorders in families identified by a schizophrenic proband (index case) has provided an indirect clue to the diagnostic boundaries of proposed spectrum categories. However, the early observations of familial aggregation of schizophrenic disorder and schizophrenic-spectrum features lacked (1) standard, blind assessment of explicit diagnostic features in relatives and (2) informative control groups for comparison of relative recurrence risks.

Squires-Wheeler et al.

Until the Danish Adoption studies of Kety, Rosenthal, and Wender (Kety, Rosenthal, Wender, & Schulsinger, 1968; Kety, Rosenthal, Wender, Schulsinger, & Jacobsen, 1975; Kety, 1983, 1985, 1987; Rosenthal, Wender, Kety, Welner, & Schulsinger, 1971; Kendler, Gruenberg, & Strauss, 1981; Kendler & Gruenberg, 1984), no spectrum category had a compelling empirical foundation. The Danish studies provided evidence for the range of phenotypic expression of a putative genotype, subsequently called schizotypal personality disorder (STPD) in DSM-III (1980) and DSM-III-R (1987). Kety (1987, 1988) has recently published results from the Danish Provincial Sample that replicates the earlier results concerning the diagnostic boundaries of the hypothesized constitutional spectrum. On the basis of these studies, Ingraham and Kety conclude: "Since the prevalence of schizophrenia spectrum disorders in the biological relatives of schizophrenic adoptees is as great as that which appears in the natural families of schizophrenic patients, the familial association of schizophrenia spectrum disorder, with classical schizophrenia must be largely the result of genetic factors" (1988, p. 123).

The utility of a valid spectrum category for research extends to questions concerning both genetic and environmental factors contributing to expression of schizophrenic disorder. If STPD is a disorder continuous with schizophrenia in terms of etiology and pathogenesis, then it can be used as an indicator of putative constitutional liability factors underlying both STPD and schizophrenic disorders. STPD and schizophrenic disorder differ in severity such that individuals with STPD express only mild schizophrenia-like signs and symptoms and, thus, are not routinely exposed to the effects of prolonged psychosis, treatment, hospitalization, or social labelling, which usually attend the diagnosis of schizophrenic disorder. With STPD as the diagnostic unit of analysis, one may avoid, for example, the contaminating effects of drug treatment when investigating physiological and biochemical correlates of the primary vulnerability. Similarly, one would avoid the effects of social labelling when examining psychological measures.

Investigation of the social, environmental, and independent constitutional correlates of "invulnerability to decompensation" may be undertaken with STPD as a diagnostic unit of analysis, thereby gaining an understanding of protective factors (Gunderson, Siever, & Spaulding, 1983). Such a study of protective or buffering factors would involve STPD subjects of middle-age, as it would be more likely that STPD is the final stable phenotypic disturbance in these individuals.

Finally, if the constitutional vulnerability is conferred through a genetic mechanism, meaningful statistical analysis of the specific genetic mode of transmission requires identification of family members with the putative schizophrenic genotype. Genetic modelling also requires a well-defined and accurately identified trait. If schizophrenic disorders and STPD are phenotypic variants, failure to include STPD in a genetic analysis may compromise genetic model-fitting approaches (Risch, 1984).

While there is some agreement concerning the potential research utility of a schizophrenicspectrum category, there is no consensus that the DSM-III and DSM-III-R STPD sets of criteria are optimal for identifying the phenotypic boundaries of a putative schizophrenic genotype. Further, there is limited information on the question of diagnostic specificity. It is

desirable to establish population rates and to establish STPD rates in families identified not only by probands with schizophrenia but also through probands with other major psychiatric disorders.

The few existing studies of specificity of STPD to families with schizophrenia have not confirmed the assumption of diagnostic specificity (Ingraham & Kety, 1987; Rosenthal, Wender, Kety, Welner, & Schulsinger, 1971; Squires-Wheeler, Skodol, Friedman, & Erlenmeyer-Kimling, 1988). Due to the potential utility of a "validated constitutional spectrum" and the contradictory results obtained to date, the study reported here is one of the necessary, independent investigations of STPD employing the use of direct, blind, and standardized diagnostic interviews. This study extends the previous inquiries by the use of a semi-structured interview to assess STPD as defined by DSM-III-R criteria. The research reported here addresses the questions of normal control prevalence rates and the diagnostic specificity of DSM-III-R schizotypal personality traits and disorder, by means of a family study.

METHODS

Subjects

The subjects of this report are offspring of schizophrenic, affectively ill and normal control parents. These subjects are drawn from two samples, A and B, collected at two different time periods, in the New York High Risk Project, a longitudinal family study (Erlenmeyer-Kimling & Cornblatt, 1987). Samples A and B have been followed since 1971 and 1978, respectively. At those times of intake, the offspring subjects were between the ages of 7 and 12 yr and were free of psychiatric impairment. Parental diagnoses first obtained at intake were later updated using the SADS-L and RDC. In this report, data on subjects from the two samples were pooled with data on siblings of these subjects, who were not part of the original study because they were younger than age 7 or older than age 12 at intake of the family into the study.

Table 1 summarizes the demographic characteristics of the sample. There are 90 offspring from the schizophrenic parent group, 79 offspring from the affective disorder parent group, and 161 offspring from the normal control parental group, ranging in age from 18 to 31 yr. These interviewed subjects represent 79% of the offspring from the schizophrenic disorder parental group, 71% of the offspring from the affective disorder parental group, and 72% of the offspring from the normal control parental group currently participating in the study. These interviewed subjects were at least 18 yr of age at the time of the interview.

Diagnostic assessments

This study employed blind, direct diagnostic assessments using the Personality Disorder Examination (PDE) (Loranger, Susman, Oldham, & Russakoff, 1985). The PDE is a standardized, semi-structured clinical interview for eliciting information relevant to the Diagnostic and Statistical Manual of Mental Disorders, Third Edition-Revised (DSM-III-R) personality disorders. The PDE was administered to subjects by clinical psychologists and social workers after a period of orientation and training in the use of the schedule. The

interviewers were trained in the use of the instrument by means of group workshops and individual supervision. The interviewers were blind to parental diagnostic status and to results of previous clinical assessments of the offspring. Interviews were conducted in the subjects' homes or in our offices and were audiotaped when consent was obtained. Subjects who could not be interviewed directly due to distance or scheduling conflicts, were interviewed by telephone (14.24% of the sample). The interview schedule and the audiotapes were reviewed by a clinical supervisor as part of the training, and were thereafter reviewed by a clinical supervisor if the interviewe received a Global Assessment of Personality score (from the Structured Clinical Interview for DSM-III-R Personality Disorders (SCID-II), 7/1/85, page 28) of poor or lower. Any disagreements concerning item scoring were resolved at a clinical conference. Table 2 outlines DSM-III-R schizotypal features assessed using the PDE.

Analyses

The group distribution of individual features was addressed by pair-wise proportion differences using Fleiss' z tests (Fleiss, 1981), with one tail significance levels. The prevalence of 2, 3, or 4 or more STPD features present by parental group status was examined by Fleiss's z test for proportion differences using age-adjusted denominators. The prevalence was assessed using both (1) number of relatives expressing STPD features and (2) number of families with at least one offspring expressing STPD features, as the units of analysis.

RESULTS

Table 3 shows the rates of individual personality features by parental diagnostic group. Significant differences between offspring of schizophrenic parents and offspring of normal control parents were found on the following features: odd behavior, inappropriate affect, odd speech, and recurrent illusions (P < 0.05). Items which differentiated offspring of affective disorder parents from normal controls at significant levels (P < 0.05) included inappropriate affect, odd speech, suspiciousness, and undue social anxiety. There were no significant differences on any feature between the offspring of parents with schizophrenic disorder and offspring of parents with affective disorder (although there is diminished power to detect significant differences given the smaller sample size of these groups).

The distributions of number of schizotypal features for each group (Table 4) show that 17.8% of the offspring of schizophrenic parent probands exhibited three or more schizotypal features; 11.4% of the offspring of affective disorder parent probands exhibited three or more schizotypal features, and 4.3% of the offspring of normal controls exhibited three or more schizotypal features.

Table 5 shows the number of offspring in each parental group exhibiting three or more features and four or more schizotypal features, and the number of families for whom at least one offspring exhibited the given number of features. The significance of the difference in rates of three or more features present between schizophrenic disorder relatives and normal control relatives is 0.0005. While there are other significant contrasts in the table, none reach a corrected significance level. The contrasts between the offspring of schizophrenic and

affective disorder parents and/or families were all insignificant, with *P* values of 0.184 or greater. When these analyses were repeated using age adjustments derived from published empirical age of onset distributions (Baron, Gruen, Asnis, & Endicott, 1980; Baron, Gruen, Asnis, & Kane, 1983a,b; Baron, Gruen, Rainer, Kane, Asnis, & Lord, 1985), the contrast between offspring of schizophrenic parents and offspring of normal controls was significant for three or more schizotypal features (Table 6). The contrast between offspring of affective disorder parents and offspring of normal controls were significant for three, four, and five more features present (at significance levels of less than 0.05). The rates seen here for offspring of affective disorder parents for three or more schizotypal features or what has been called probable and definite schizotypal personality disorder (Baron *et al.*, 1985), ranged from 8% to 14.5%.

DISCUSSION

The elevated rates of schizotypal features and disorder among the relatives (offspring) of schizophrenic index cases is consistent with previous reports. In Kendler's (1988a,b) review, rates of probable and definite schizotypal personality disorder in relatives of schizophrenic disorder index cases ranged from 5 to 34%. The use of DSM-III-R criteria and the direct interview assessments using the PDE appear to be sufficiently sensitive. In this study the offspring of affective disorder parents exhibited rates for schizotypal features that were as high as some of those published previously for relatives of schizophrenic disorder probands.

This pattern of results is similar to an earlier finding from an assessment conducted more than six years ago of a subsample of Sample A offspring (Squires-Wheeler et al., 1988). When the Sample A subjects were between the ages of 15 and 21, schizotypal features were evaluated by at least two independent raters from videotapes of a semi-structured clinical interview. DSM-III criteria for schizotypal features were used. The psychiatrists who conducted the interview and the psychiatric residents who rated the schizotypal features were blind to parental diagnoses. There was no significant difference between the rates of three or more schizotypal features in the offspring of affective disorder parents (23.1%) and the offspring of schizophrenic disorder parents (12.5%). Normal control rates were 3.6%. When comparing the two longitudinal assessments, the rates for three or more schizotypal features are increasing in the offspring from the schizophrenic disorder parental group, relative to the rates in the offspring from the affective disorder parental group. That is, in the current assessment, the respective rates are 17.8% and 11.4% for the offspring from the schizophrenic disorder and affective disorder parental groups. The rates for four or more features remain constant and nonspecific. Five per cent and 6.7% of the offspring from the schizophrenic disorder parental group exhibited 4 or more STPD features in the early and current assessments, respectively, while 8.6% and 8.9% of the offspring from the affective disorder parental group exhibited 4 or more STPD features in the early and current assessments, respectively. The rates of 4 or more STPD features in the early and current assessments for the offspring from the normal control parental group was 1.2% and 2.5%, respectively.

These results are also consistent with a recent finding by Ingraham and Kety (1987) of increased rates of schizophrenic spectrum traits and disorder in first-degree relatives of

affective disorder probands. In contrast, however, Coryell and Zimmerman (1988) found no elevation in rates (1.9%) for schizotypal and/or paranoid personality disorder in first-degree relatives of psychotic major depression probands. They found rates of 7.6%, 5.6%, and 2.5% in relatives of schizoaffective (depressed), schizophrenic, and never ill index cases respectively.

Limitations

Reasons for the failure to demonstrate specificity may include (1) measurement error in offspring STPD assessment, (2) measurement error in parental diagnosis, or (3) lack of precision of DSM-III-R criteria to identify schizophrenic-spectrum clinical features.

It has been suggested that offspring of parents with affective disorders may be rated positive on schizotypal features exhibited in the service of affective disturbance or distress. For example, peer isolation in these offspring may be due to (intense but temporary) interpersonal conflicts (instead of social indifference or lack of social pleasure or competence). In the absence of an informant report to corroborate the self-report in the interview, or in the absence of longitudinal measurement, "false-positive assessment" described above cannot be ruled out. (One approach to exploring this possibility was undertaken at the time of the previous assessments (Sample A, Time 3).) In these videotaped interviews the coexistence of potentially distorting affective states such as depression or anger were assessed and were found to be equally prevalent among offspring expressing schizotypal features from both parental groups and hence could not be used as covariates to distinguish offspring with schizotypal features from the respective parental diagnostic groups. Nonetheless this affective symptom covariate analyses could be undertaken in subsequent clinical interviews to provide the basis for a potentially differentiating clinical profile.

Further limitations of the assessment here include the cross-sectional interviews and the use of telephone interviews in a subset of subjects. While the interviewer stressed that the interview concerned "what you are like most of the time ... what has been typical of you throughout your life and not just recently," a cross-sectional assessment of a putative trait is limited by potential distortion due to state factors. The most convincing assessment would involve longitudinal measurement and informant collateral reports. It is also apparent that a telephone interview is a compromised context for measurement of a clinical syndrome for which observational data is important, e.g., in the assessment of inadequate rapport. Ten per cent of offspring from the schizophrenic disorder parental group, 7.6% of the offspring from the affective disorder parental group, and 19.8% of the offspring from the normal control parental group were assessed by telephone interviews. It is known that sensitivity is diminished in the assessment of psychiatric conditions when a telephone interview is used.

The parental diagnoses have been reviewed and updated as diagnostic criteria have evolved (i.e., DSM-III, 1980, and DSM-III-R, 1987) since 1971, with the assistance of the New York State Psychiatric Biometrics Division. However, important diagnostic complications such as parental index case clinical comorbidity, assortive mating (for psychiatric disorder in general), and the presence of psychiatric disorder in the second degree relatives of the offspring (the parents and siblings of the parent probands) may be important factors in

Squires-Wheeler et al.

expression of schizotypal features in the study offspring. A family study and a family history study is underway and will provide a more comprehensive account of parental clincial status.

Criteria for DSM-III and DSM-III-R schizotypal features and disorder represent a best guess based on compelling evidence from the Danish Adoption Studies. The implicit principle for adducing schizophrenic spectrum criteria has been voiced by Kendler (1985). "... Criteria proposed for schizotypal personality disorder should have maximal sensitivity and specificity in identifying relatives of schizophrenic patients." Kety (1985) has stated, "the genetic relationship of schizotypal personality disorder (or the latent and uncertain schizophrenias on which it was based) to paradigmatic schizophrenia is clearly demonstrated by their high prevalence in the biological relatives of adoptees with chronic schizophrenia." Kety also notes that "schizotypal personality disorder of DSM-III is only a first approximation to (Bleuler's 'latent schizophrenia')". This suggests a complementary but independent research goal to the goal of replication defined above. Independent exploratory studies are also needed to provide alternative constructions of the schizophrenic spectrum. As Kety has concluded, "there are undoubtedly many more characteristics of the nonpsychotic genotypes of schizophrenia which remain to be noted and evaluated."

Required next steps

An examination of the critical question of stability of expression of schizotypal features is underway. Additional complexities which must be examined before a definitive conclusion concerning STPD diagnostic specificity (or lack of specificity) include examination of parental comorbidity, offspring comorbidity, and parental assortative mating. Assessment directed toward these questions is currently underway. Furthermore, due to the small sample size and the relatively young age of the offspring examined in this report, conclusions from these siblings must be tentative. Continued follow-up is required to examine the natural history of such features.

However, these findings do suggest a cautionary note regarding the use of DSM-III-R schizotypal features and disorder as an indicator of a putative vulnerability indicator specific to schizophrenic disorder. For example, with respect to linkage studies of psychiatric disorders in general, Morton and Kidd note: "It is absolutely critical for the assignment of recombinant/nonrecombinant status to individuals in a pedigree that we know which of the diagnoses present are likely to represent alternate manifestations of the … genotype and which are likely to represent other genetic or nongenetic entities" (1980). They also note that some spectrum candidates may occur at relatively high rates in the general population. This means that such spectrum diagnoses are likely to "occur sporadically in large pedigrees by chance alone" (1980). Thus further investigation of the distribution of schizotypal traits and disorder in demographically defined normal control and psychiatric control populations is important for optimal use of such traits and disorder in genetic linkage analysis (St. Clair, Blackwood, Muir, Baillie, Hubbard, Wright, & Evans, 1989; Sherrington, Brynjolfsson, Petursson, Potter, Dudleston, Barraclough, Wasmuth, Dobbs, & Gurling, 1988).

References

- American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 3. American Psychiatric Association; Washington, DC: 1980.
- American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 3. American Psychiatric Association; Washington, DC: 1987. revised
- Baron Gruen, R., Asnis, L., Endicott, J. Schedule for Interviewing Borderlines (SIB). New York: New York State Psychiatric Institute; 1980.
- Baron M, Gruen R, Asnis L, Kane J. Age-of-onset of schizophrenia and schizotypal disorders: clinical and genetic implications. Neuropsychobiology. 1983a; 10:199–204. [PubMed: 6676674]
- Baron M, Gruen R, Asnis L, Kane J. Familial relatedness of schizophrenia and schizotypal states. American Journal of Psychiatry. 1983b; 140:1437–1442. [PubMed: 6624988]
- Baron M, Gruen R, Ranier JD, Kane J, Asnis L, Lord S. A family study of schizophrenic and normal control probands: implications for the spectrum concept of schizophrenia. American Journal of Psychiatry. 1985; 142:447–455. [PubMed: 3976917]
- Bleuler, E. Dementia Praecox, or the Group of Schizophrenias 1911. Zinkin, J., translator. New York: International University Press; 1950.
- Coryell W, Zimmerman M. The heritability of schizophrenia and schizoaffective disorder. Archives of General Psychiatry. 1988; 45:323–327. [PubMed: 3355319]
- Erlenmeyer-Kimling L, Cornblatt B. The New York High Risk Project: A Follow-up Report. Schizophrenia Bulletin. 1987; 13:451–461. [PubMed: 3629200]
- Essen-Moller, E. The concept of schizoidia. In: Kloesi, J., editor. Psychiatrie und Neurologie. Vol. 112. Basel: Karger; 1946. p. 258-271.
- Fleiss, JL. Wiley Series in Probability and Mathematical Statistics. 2. New York: Wiley and Sons; 1981. Statistical Methods for Rates and Proportions.
- Frangos E, Athanassenas G, Tsitourides S, Katsanou N, Alexandrakou P. Prevalence of DSM-III schizophrenia among the first-degree relatives of schizophrenic probands. Acta Psychiatrica Scandinavica. 1985; 72:382–386. [PubMed: 4072739]
- Gunderson JG, Siever L, Spaulding E. The search for a schizotype: crossing the border again. Archives of General Psychiatry. 1983; 40:15–22. [PubMed: 6849615]
- Heston L. The genetics of schizophrenia and schizoid disease. Science. 1970; 167:249–256. [PubMed: 4902547]
- Hollingshead, AB., Redlich, FC. Social Class and Mental Illness. New York: Wiley and Sons; 1958.
- Ingraham, LJ., Kety, SS. Schizophrenia spectrum disorders. In: Nasrallah, AH., editor. Handbook of Schizophrenia, Volume 3: Nosology, Epidemiology and Genetics of Schizophrenia. Amsterdam: Elsevier; 1988. p. 117-137.
- Ingraham, LJ., Kety, SS. Schizophrenia Spectrum Disorders: Exclusively Related to Schizophrenia?. Poster presented at the International Congress on Schizophrenia Research; 28 March–1 April 1987; 1987.
- Kendler KS. Diagnostic approaches to Schizotypal Personality Disorder: a historical perspective. Schizophrenia Bulletin. 1985; 2:538–553.
- Kendler, KS. The genetics of schizophrenia and related disorders: A Review. In: Dunner, DL.Gershon, ES., Barrett, JE., editors. Relatives at Risk for Mental Disorder. New York: Raven Press; 1988a. p. 247-266.
- Kendler KS. Familial aggregation of schizophrenia and schizophrenia spectrum disorders. Archives of General Psychiatry. 1988b; 45:377–383. [PubMed: 3281628]
- Kendler KS, Gruenberg AM. An independent analysis of the Danish adoption study of schizophrenia: VI. the relationship between psychiatric disorders as defined by DSM-III in the relatives and adoptees. Archives of General Psychiatry. 1984; 41:555–564. [PubMed: 6732417]
- Kendler KS, Gruenberg AM, Strauss JS. An independent analysis of the Copenhagen sample of the Danish adoption study of schizophrenia, II. The relationship between schizotypal personality disorder and schizophrenia. Archives of General Psychiatry. 1981; 38:982–984. [PubMed: 7283669]

- Kety, SS., Rosenthal, D., Wender, PH., Schulsinger, F., Jacobsen, B. Mental illness in the biological and adoptive families of adopted individuals who have become schizophrenic: a preliminary report based on psychiatric interviews. In: Fieve, RR.Rosenthal, D., Brill, H., editors. Genetic Research in Psychiatry. Baltimore: Johns Hopkins University Press; 1975. p. 147-165.
- Kety SA. Mental illness in the biological and adoptive relatives of schizophrenic adoptees; findings relevant to genetic and environmental factors in etiology. American Journal of Psychiatry. 1983; 140:720–727. [PubMed: 6342426]
- Kety SS. Schizotypal personality disorder: an operational definition of Bleuler's latent schizophrenia? Schizophrenia Bulletin. 1985; 2:590–594.
- Kety SS. The significance of genetic factors in the etiology of schizophrenia: results from the National Study of Adoptees in Denmark. Journal of Psychiatric Research. 1987; 21:423–429. [PubMed: 3440955]
- Kety SS. Schizophrenic illness in the families of schizophrenic adoptees: findings from the Danish National Sample. Schizophrenia Bulletin. 1988; 14:217–222. [PubMed: 3201179]
- Kety SS, Rosenthal D, Wender PH, Schulsinger F. The types and prevalence of mental illness in biological and adoptive families of adopted schizophrenics. Journal of Psychiatric Research. 1968; 6:345–362.
- Loranger AW, Susman VL, Oldham JM, Russakoff LM. The Personality Disorder Examination: a preliminary report. Journal of Personality Disorders. 1987; 1:1–13.
- Meehl PE. Schizotaxia, schizotypy, schizophrenia. American Psychologist. 1962; 1:827–838.
- Morton LA, Kidd KK. The effects of variable age-of-onset and diagnostic criteria on the estimates of linkage: an example using manicdepressive illness and color blindness. Social Biology. 1980; 27:1–10. [PubMed: 6974894]
- Rado, S. Theory and therapy: the theory of schizotypal organization and its application to the treatment of decompensated schizotypal behavior. In: Scher, SC., Davis, HR., editors. The Out-Patient Treatment of Schizophrenia. New York: Grune & Stratton; 1960. p. 87-101.
- Risch N, Baron M. Segregation analysis of schizophrenia and related disorders. American Journal of Human Genetics. 1984; 26:1039–1059.
- Rosenthal D, Wender PH, Kety SS, Welner J, Schulsinger F. The adopted away offspring of schizophrenics. American Journal of Psychiatry. 1971; 128:307–311. [PubMed: 5570995]
- Sherrington R, Brynjolfsson J, Petursson H, Potter M, Dudleston K, Barraclough B, Wasmuth J, Dobbs M, Gurling H. Localization of a susceptibility locus for schizophrenia or chromosome 5. Nature. 1988; 336:164–167. [PubMed: 2903449]
- Shields, J., Heston, LL., Gottesman, II. Schizophrenia and the schizoid: the problems for genetic analysis. In: Fieve, RR.Rosenthal, D., Brill, H., editors. Genetic Research in Psychiatry. Baltimore: The Johns Hopkins University Press; 1975. p. 167-197.
- Spitzer, RL., Endicott, J., Robins, E. Research Diagnostic Criteria (RDC). Biometrics Research Department, New York State Psychiatric Institute; New York: 1978.
- Spitzer, RL., Williams, JBW. Structured Clinical Interview for DSM-III-R Personality Disorders (SCID II, 7/1/85). Biometrics Research Department, New York State Psychiatric Institute; New York: 1985.
- Squires-Wheeler E, Skodol AE, Friedman D, Erlenmeyer-Kimling L. The specificity of DSM-III schizotypal personality traits. Psychological Medicine. 1988; 18:757–765. [PubMed: 3186874]
- St Clair D, Blackwood D, Muir W, Baillie D, Hubbard A, Wright A, Evans HJ. No linkage of chromosome 5q11–q13 markers to schizophrenia in Scottish families. Nature. 1989; 339:305–309. [PubMed: 2725644]

CIHR Author Manuscript

Squires-Wheeler et al.

Table 1

Demographic characteristics of sample: Age and social class by group

			ward to Smide			
Characteristic	Schizophrenic di	sorder $(N = 90)$	Affective diso	rder $(N = 79)$	No disorder	* $(N = 161)$
Age yr	N	(%)	N	(%)	N	(%)
18-20	19	(21.1)	21	(26.6)	46	(28.6)
21–22	17	(18.9)	18	(22.8)	38	(23.6)
23–24	19	(21.1)	15	(19.0)	28	(17.4)
25-26	17	(18.9)	13	(16.5)	25	(15.5)
27–28	8	(8.9)	8	(10.1)	13	(8.1)
29+	10	(11.1)	4	(5.1)	11	(6.8)
		Soci	al Class			
Hollingshead & F	Redlich Index					
1 Highest	7	(7.8)	1	(1.3)	23	(14.3)
2	1	(1.1)	0	(0.0)	25	(15.5)
3	8	(8.9)	22	(27.8)	30	(18.6)
4	99	(73.3)	48	(60.8)	79	(49.1)
5 Lowest	8	(8.9)	8	(10.1)	4	(2.5)

Table 2

DSM-III-R features for schizotypal Personality Disorder

1	Ideas of reference (excluding delusions of reference)
2	Excessive social anxiety, e.g. extreme discomfort in social situations involving unfamiliar people
3	Odd beliefs or magical thinking, influencing behavior and inconsistent with subcultural norms, e.g., superstitiousness, belief in clairvoyance, telepathy, or "sixth sense," "others can feel my feelings" (in children and adolescents, bizarre fantasies or preoccupations)
4	Unusual perceptual experiences, e.g., illusions, sensing the presence of a force or person not actually present (e.g., "I felt as if my dead mother were in the room with me")
5	Odd or eccentric behavior or appearance, e.g., unkempt, unusual mannerisms, talks to self

- No close friends or confidants (or only one) other than first-degree relatives 6
- 7 Odd speech (without loosening of associations or incoherence), e.g., speech that is impoverished, digressive, vague, or inappropriately abstract
- Inappropriate or constricted affect, e.g. silly, aloof, rarely reciprocates gestures or facial expressions, such as smiles or nods 8
- 9 Suspiciousness or paranoid ideation

CIHR Author Manuscript

Table 3

DSM-III-R Schizotypal Personality Disorder features in offspring of schizophrenic disorder probands, affective disorder probands, and normal controls diagnosed by the personality disorder examination

Squires-Wheeler et al.

	Schizophrenic disord	ler probands (90)	Affective disorder	r probands (79)	Normal Contr	ols (161)
	Ν	(%)	Ν	(%)	Ν	(%)
Social isolation	20	22.2	15	19.0	24	14.9
Odd speech	7	7.8 <i>†</i>	4	5.1^{*}	1	9.
Inappropriate affect	17	18.9 t	12	15.2^{*}	8	5.0
Odd behavior or appearance	8	8.9%	5	6.3	3	1.9
Suspiciousness	13	14.4	17	21.5*	12	7.5
Ideas of reference	6	10.0	L	8.9	7	4.3
Undue social anxiety	7	7.8	14	17.7^{*}	12	7.5
Magical thinking	×	8.9	5	6.3	12	7.5
Recurrent illusions	10	11.1^{\neq}	7	8.9	5	3.1

 $\stackrel{f}{\not }$ Offspring of schizophrenic disorder probands versus offspring of normal controls. P<0.05.

Table 4

Number of DSM-III-R schizotypal Personality Disorder features present in offspring by parental diagnostic group

			4	Number of	features pre	sent		
		0	1	7	3	4	Ś	6 +
Schizophrenic parental group $N = 90$	N(%)	43 (47.8)	22 (24.4)	9 (10.0)	10 (11.1)	3 (3.3)	2 (2.2)	1 (1.1)
Affective parental group $N = 79$	N(%)	38 (48.1)	23 (29.1)	9 (11.4)	2 (2.5)	2 (2.5)	1 (1.3)	4 (5.1)
Normal control parental group $N = 161$	N(%)	108 (67.1)	36 (22.4)	10 (6.2)	3 (1.9)	3 (1.9)	0 (0.0)	1 (0.6)

Squires-Wheeler et al.

-
()
<u> </u>
т
二
λ
2
$\mathbf{\Sigma}$
2
=
÷
2
2
>
\geq
С С
5
Ζ.
5
0
0
Ξ.
0
<u> </u>

CIHR Author Manuscript

Squires-Wheeler et al.

Table 5

Proportion of offspring exhibiting schizotypal features by Parental Diagnostic Group

Schizotypal personality disorder criteriaSchizophrenic parental group (A)Affective disorder parental group (B)Normal control parental group (C)Significance of proportion differ (C)Three or more schizotypal features (offspring) $16/90 (17.8\%)$ $9/79 (11.4\%)$ $7/161 (4.3\%)$ 0.184 0.0005^* 0.1 Three or more schizotypal features (families) \mathring{r} $9/39 (23\%)$ $5/31 (16.1\%)$ $5/59 (8.5\%)$ 0.345 0.045 0.115 0.115 0.115 Four or more schizotypal features (families) \mathring{r} $6/90 (6.7\%)$ $7/79 (8.9\%)$ $4/161 (2.5\%)$ 0.421 0.115 0.1045	Schizotypal personality disorder criteria (A)					
A vs B A vs C B Three or more schizotypal features (offspring) 16/90 (17.8%) 9/79 (11.4%) 7/161 (4.3%) 0.184 0.0005 * 0. Three or more schizotypal features (families) \mathring{r} 9/39 (23%) 5/31 (16.1%) 5/59 (8.5%) 0.345 0.045 0. Four or more schizotypal features (families) 6/90 (6.7%) 7/79 (8.9%) 4/161 (2.5%) 0.421 0.115 0.		group Affective disorder parental group (B)	Normal control parental group (C)	Significanc	e of proportion	ı difference ⁵
Three or more schizotypal features (offspring) 16/90 (17.8%) $9/79 (11.4\%)$ $7/161 (4.3\%)$ 0.184 0.0005^* 0.184 Three or more schizotypal features (families) \dot{r} $9/39 (23\%)$ $5/31 (16.1\%)$ $5/59 (8.5\%)$ 0.345 0.045 0.115 Four or more schizotypal features (offspring) $6/90 (6.7\%)$ $7/79 (8.9\%)$ $4/161 (2.5\%)$ 0.421 0.115 0.115				A vs B	A vs C	B vs C
Three or more schizotypal features (families) \mathring{r} 9/39 (23%) 5/31 (16.1%) 5/59 (8.5%) 0.345 0.045 0. Four or more schizotypal features (offspring) 6/90 (6.7%) 7/79 (8.9%) 4/161 (2.5%) 0.421 0.115 0.	Three or more schizotypal features (offspring) 16/90 (17.8%)	9/79 (11.4%)	7/161 (4.3%)	0.184	0.0005^{*}	0.045
Four or more schizotypal features (offspring) 6/90 (6.7%) 7/79 (8.9%) 4/161 (2.5%) 0.421 0.115 0.	Three or more schizotypal features (families) $\dot{\tau}$ 9/39 (23%)	5/31 (16.1%)	5/59 (8.5%)	0.345	0.045	0.242
	Four or more schizotypal features (offspring) 6/90 (6.7%)	7/79 (8.9%)	4/161 (2.5%)	0.421	0.115	0.036
	Four or more schizotypal features (families) 5/39 (12.8%)	5/31 (16.1%)	3/59 (5.1%)	0.50	0.184	0.097

 \sharp Table entries under each group are proportions exhibiting indicated number of features.

 $\stackrel{f}{\not\sim}$ Proportion of families with at least one adolescent affected.

** for a = 0.05 and 12 tests; P = 0.004

 $\overset{\mbox{\scriptsize S}}{}$ Fleiss's (1981) z statistic of proportion difference (one tail significance levels).

Proportion of offspring exhibit	ing schizotypal personality disord	er features (age adjusted) by	/ Parental Diagnostic Group			
		Group proportion with di	isorder present † —age adjusted			
Schizotypal personality disorder criteria	Schizophrenic parental group (A)	Affective disorder parental group (B)	Normal control parental group (C)	Significano	ce of proportior	difference \ddagger
				A vs B	A vs C	B vs C
Three or more schizotypal features (offspring)	16/73 (22%)	9/62 (14.5%)	7/125 (5.6%)	0.20	0.0007*	0.036
Four or more schizotypal features (offspring)	7/73 (8.2%)	7/62 (11.3%)	4/125 (3.2%)	0.384	0.115	0.036
Five or more schizotypal features (offspring)	3/73 (4.1%)	5/62 (8%)	1/125 (.8%)	0.25	0.15	0.139

Probability level for "multiple independent tests"=1 – $(1-\alpha)$

* for a = 0.01 and 9 tests; P = 0.0011

** for a = 0.05 and 9 tests; P = 0.0056

 $\stackrel{f}{\tau}$ Table entries under each group are proportions exhibiting indicated number of features.

 \star^{t} Fleiss's (1981) z statistic of proportion difference (one tail significance levels).

Table 6