Eur Arch Psychiatry Clin Neurosci (1990) 240:16–20

European Archives of Psychiatry and Clinical Neuroscience

Familial Rates of Affective Illness in Sardinia with Special Reference to Schizoaffective Disorder*

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Received February 16, 1990

Summary. Familial rates of psychiatric disorders were studied in southern Sardinia and showed an increase in relatives of probands with the following research diagnostic criteria (RDC) diagnoses: normal, unipolar depression, schizoaffective depressive, schizoaffective bipolar, bipolar with mania and bipolar with hypomania. A significantly higher risk for bipolar schizoaffective disorder was observed in relatives of bipolar schizoaffectives compared with relatives of normal probands.

Key words: Affective disorders – Schizoaffective disorders – Bipolar – Unipolar – Familial rates

Introduction

One of the various uses of the studies of families with psychiatric disorders is to help define nosological entities and identify characteristics associated with increased morbid risk. We studied first-degree ($n = 1485$) relatives of 209 probands, collected at an outpatient facility in southern Sardinia. The nature of our proband sample, which included 82 schizoaffective (SA), 38 bipolar I (BP-I), 27 bipolar II (BP-II) and 29 unipolar (UP) patients, as well as 33 psychiatrically normal controls, led us to focus on SA disorder.

Subjects and Methods

Patients admitted to the outpatient clinics for affective disorders of the Department of Neurosciences, University of Cagliari were screened concurrently with their admission from 1985 to 1988.

Admission to the clinics and selection for this study were independent of family history. Patients admitted over the previous 10 years were also screened if they were still attending the clinics. No patients related to each other were ascertained independently. We independently applied our diagnostic criteria to medical records, direct interview, and information from relatives about each proband. Normal control probands were university employees who had no history of diagnosable psychiatric disorder. All probands gave informed consent to participate in the study and permitted the participation of their relatives.

Modified research diagnostic criteria (RDC) were applied uniformly to all data regarding probands and relatives (older than 17 years). A hierarchical lifetime diagnosis was created according to the following order: schizophrenia; SA disorder, bipolar subtype (SA-B); SA disorder, depressive subtype only (SA-D); bipolar I disorder; bipolar II disorder; unipolar major depressive disorder. Individuals with a diagnosis of SA disorder, manic (or mixed) subtype, and individuals with diagnoses of both SA-D and BP-I were included as having SA-B. Individuals with a diagnosis of mania (or hypomania) without an additional diagnosis of depression were classified as having BP-I (or BP-II). Patients with only drug-induced hypomania were included as having BP-II. Impairment of functioning in the major life role had to be present for the diagnosis of major depressive disorder. Consensus diagnoses in relatives were made blind to the proband diagnoses, using all available sources. Initial information on pedigree and family history were obtained from the proband. Family history was collected from at least one additional informant in about 20% of families. Diagnosis in affected relatives was based on information from at least two relatives in 31 cases (including 9 deceased), and from one relative in 89 cases (including 24 deceased). A reliable diagnosis was not reached in 8 cases owing to unsatisfactory information. Records of psychiatric hospitalizations, ambulatory visits (mostly at lithium clinics), or both were available for 21, 25 and 12 relatives, respectively. In particular, 76% (38/50) of the diagnoses higher on the hierarchy (schizophrenia, SA-B, SA-D, BP-I, or BP-II) were also based on record information. Among the 222 affected relatives, 73 were personally interviewed. Overall, we personally interviewed 207 out of 1211 living relatives.

Characteristics of the Probands and Relatives. Table 1 shows some characteristics of the sample. The proband groups were comparable for sex, family size and sex ratio in relatives. The differences in the mean ages at the time of the study may be important, since birth cohorts can influence data on age at onset. The considerable number of years since onset of illness is noteworthy, particularly in view of the longitudinal assessment of bipolarity and schizoaffectivity.

* Supported by a grant from Regione Autonoma della Sardegna, Assessorato all'Igiene e Sanità

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Age Correction and Risk in Relatives. As we are combining data from multiple generations and changes over time in the age-specific risks for psychiatric disorders have been reported, our data are presented either as actual raw numbers or using traditional methods of age correction to enable comparison with existing published data.

Table 1. Characteristics of the sample

Diagnosis	No.	Current age (years) (mean ± SD)	Years of illness (mean ± SD)	No. of relatives (age 18 years and older)		
				Parents	Siblings	Children
SA-B	56	39.8 ± 11.1	14.1 ± 8.7	112	223	41
SA-D	26	42.2 ± 10.7	16.5 ± 10.1	52	120	18
BP-I	38	54.8 ± 15.7	21.7 ± 14.8	76	183	43
BP-II	27	49.8 ± 13.9	19.0 ± 9.4	54	113	25
UP	29	55.7 ± 11.5	21.9 ± 9.4	58	120	61
Normal	33	40.4 ± 10.6	–	66	102	18

SA-B, Schizoaffective disorder, bipolar subtype; SA-D, schizoaffective disorder, depressive subtype; BP-I, bipolar I; BP-II, bipolar II; UP, unipolar

Table 2. Age at onset in probands and affected relatives

Diagnosis	No.	Age at onset (years) ($\log_e$ ± SD)	Median age (years)
SA	105	3.15 ± 0.31 (a)	23
BP	83	3.35 ± 0.40 (b)	29
UP, women	57	3.44 ± 0.39 (c)	31
UP, men	24	3.66 ± 0.43 (d)	39

Significance, Student's *t*-test: (a) < (b) and (a) < (c + d) ($P < 0.01$); (b) < (c + d) ($P < 0.02$); (c) < (d) ($P < 0.05$)
For abbreviations, see Table 1

Age corrected rates among the relatives were calculated by a modification of Stromgren's method, which weights the number of persons at risk by the proportion of the risk period through which they have passed. The corrected number at risk was determined by adding the proportion of risk already passed for each subject in each group according to the mean and SD of the $\log_e$ age of onset for the disorder among probands and relatives in this study. Corrected rates were then calculated by dividing the number of affected in each group by the corrected number at risk for that group. There were no significant differences in age at onset between probands and ill relatives with the same hierarchical diagnosis. The ages at onset for SA-B and SA-D did not differ from each other, but were significantly lower than for BP ($P < 0.01$) or UP ($P < 0.01$). There were no differences between BP-I and BP-II, while the age at onset for BP was significantly lower than for UP ($P < 0.02$). The only sex difference was found for UP, men showing a significantly later age at onset than women ($P < 0.05$). Overall, we used four separate functions (Table 2) in computing the number of relatives at risk for each disorder.

The statistical comparison of either the unadjusted rates or the morbid risks for psychiatric disorders in the groups of relatives was calculated by means of the difference in proportions as modified by Breborowicz and Trzebiatowska-Trzeciak (1976).

Results

Illness Rates in First-Degree Relatives

We report our data on psychiatric disorders among first-degree relatives in terms of actual numbers and percentages in Table 3, and in terms of age-adjusted rates in Table 4. The results were essentially in the same direction. The overall rates of psychiatric disorders showed an increase in relatives of the following groups of probands: normal controls, 8.1%; UP, 9.2%; SA-D, 13.7%; SA-B, 14.4%; BP-I, 20.5%; and BP-II, 22.4%.

The same order was observed for age-adjusted rates of all major affective disorders in relatives: normal controls, 4.4%; UP, 5.3%; SA-D, 5.7%; SA-B, 10.2%;

Table 3. Rates of psychiatric disorders in relatives

	Diagnosis in probands (No. of relatives)					
	SA-B (376)	SA-D (190)	BP-I (302)	BP-II (192)	UP (239)	Normal (186)
Diagnosis in relatives, No., (%)						
SA-B	11 (2.9)[a]	0 (0.0)	4 (1.3)	3 (1.6)	1 (0.4)	0 (0.0)
SA-D	2 (0.5)	1 (0.5)	0 (0.0)	2 (1.0)	0 (0.0)	1 (0.5)
Schizophrenia, acute	1 (0.3)	1 (0.5)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
Schizophrenia, chronic	2 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)
BP-I	2 (0.5)	3 (1.6)	6 (2.0)	3 (1.6)	0 (0.0)	0 (0.0)
BP-II	0 (0.0)	0 (0.0)	3 (1.0)	2 (1.0)	0 (0.0)	0 (0.0)
UP	14 (3.7)	4 (2.1)	18 (6.0)	13 (6.8)	8 (3.3)	5 (2.7)
Minor depression	13 (3.5)	11 (5.8)	10 (3.3)	10 (5.2)	12 (5.0)	4 (2.2)
Personality disorders	2 (0.5)	4 (2.1)	7 (2.3)	5 (2.6)	0 (0.0)	1 (0.5)
Alcoholism, drug abuse	3 (0.8)	2 (1.1)	7 (2.3)	1 (0.5)	0 (0.0)	0 (0.0)
Organic	0 (0.0)	0 (0.0)	6 (2.0)	1 (0.5)	1 (0.4)	2 (1.1)
Unknown	4 (1.1)	0 (0.0)	0 (0.0)	3 (1.6)	0 (0.0)	1 (0.5)

[a] Significantly different from relatives of SA-D probands ($P < 0.01$) or normal probands ($P < 0.01$)
For abbreviations, see Table 1

Table 4. Age-adjusted rates of affective disorders in relatives

	Diagnosis in probands					
	SA-B	SA-D	BP-I	BP-II	UP	Normal
No. of relatives at risk						
SA	329.9	170.2	279.6	176.3	216.6	168.6
BP	289.2	148.4	253.2	159.9	193.9	148.2
UP	250.7	127.7	223.9	142.8	166.8	130.5
Risk, %, in relatives						
SA-B	3.3[a]	0.0	1.4	1.7	0.5	0.0
SA-D	0.6	0.6	0.0	1.1	0.0	0.6
BP-I	0.7	2.0	2.4	1.9	0.0	0.0
BP-II	0.0	0.0	1.2	1.3	0.0	0.0
UP	5.6	3.1	8.0	9.1	4.8	3.8

[a] Significantly different from relatives of SA-D probands ($P<0.01$) or normal probands ($P<0.01$)
For abbreviations, see Table 1

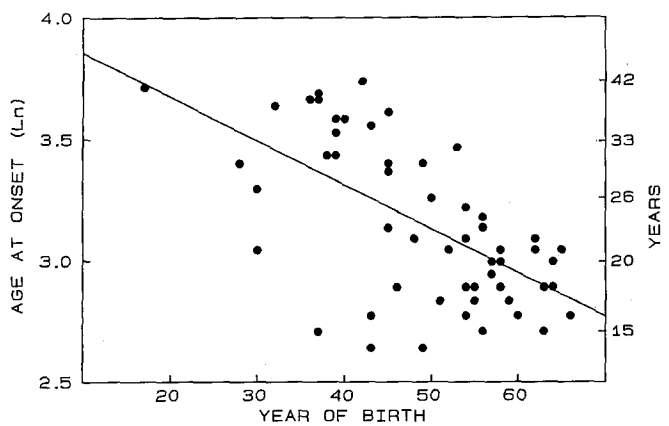

Fig. 1. Acceleration of onset in later-born cohorts of bipolar schizoaffective probands. The $\log_e$ age at onset is estimated by the linear combination $4.04 \pm 0.16 - 0.018 \times$ birth cohort (coded as the two-digit year of birth). $r = -0.61$

BP-I, 13.0%; BP-II, 15.1%. Depression aggregated in the families of all groups of affected probands. Significantly higher age-adjusted risks of UP (depression with impairment-incapacitation) were even found in relatives of bipolar (SA-B, BP-I, or BP-II) than non-bipolar (SA-D or UP) probands (7.9% vs 4.4%; $P<0.05$). Likewise, there was a trend for higher rates of suicide (whatever the diagnosis) in relatives of bipolar probands (data not shown).

The overall rates of disorders with a bipolar course (including SA-B) were similar in relatives of each group of bipolar probands, but significantly lower in relatives of non-bipolar probands (bipolar, 3.9%; non-bipolar, 0.9%; $P<0.01$). There were low rates of schizophrenia in relatives of all groups. The probands with SA-B had the highest rates of schizophrenic symptoms in relatives, significantly higher than normal probands (4.3% vs 1.1%; $P<0.05$). This was mostly due to secondary cases of SA-B illness.

There was a significantly higher percentage of women than men with psychiatric disorders among relatives (women, 18.1%; men 11.8%; $P<0.01$). Such a sex effect was mostly due to depressive disorders and was evident in both parents and siblings of probands. Other conditions such as alcoholism, drug abuse and personality disorders were significantly more frequent in male than female relatives (men, 3.0%; women, 1.4%; $P<0.05$). No sex differences in rates of bipolar or SA disorders were observed in relatives. The overall rates of psychiatric disorders in relatives of men compared with relatives of women did not significantly differ from each other. However, the sex ratio of illness in relatives of affected male probands was opposite to the general trend, mostly due to the fact that the rate of UP was higher in brothers than in sisters of male probands. Four cases of apparent father-to-son transmission of major affective disorder were observed (one each of the following pairs: BP-I/BP-I; BP-I/BP-II; BP-II/SA-B; UP/BP-II).

SA Disorder

As already shown, the subdivision of SA probands by polarity produced differences of morbid risk for affective disorders in relatives, in the direction observed between relatives of BP and UP probands. Moreover, while SA-B disorder clustered in the families of SA-B probands, relatives of SA-D probands showed a trend for increased rates of other conditions, such as minor depression, personality disorder and substance abuse. Single pedigrees with multiple cases included in some instances SA only, or both SA and pure affective, or, in a few cases, also acute or chronic schizophrenia. Secondary SA cases were observed either in siblings only or across two or three generations.

The ages at onset for SA-B and SA-D did not differ from each other, but were significantly lower than for BP or UP (see Table 2). However, this might depend in part on the relatively low mean ages of our SA probands (see Table 1). In fact, we found an accelerated onset in later-born cohorts of probands of each diagnostic group. An example is given in Fig. 1, showing that the median age at onset for SA-B probands born in 1960 would be 19 years, whereas the median for those born in 1930 would be 33 years. According to this model, the age at onset for SA in our sample would no longer differ from BP or UP. However, data on relatives who represent a wider range of birth cohorts compared with probands appear to confirm differences in age at onset, particularly with regard to the late onset of UP in men and the early onset of SA. Moreover, while a correlation in the age at onset was observed between the SA probands and their respective SA relatives, even if belonging in some cases to quite different birth cohorts (SA/SA pairs, $n = 14$; $r = 0.72$; $P<0.01$), the correlation was not found when the proband and the relative were discordant by diagnosis (e.g. SA/BP pairs, $n = 14$; $r = 0.06$).

On the other hand, a trend towards increased rates of affective disorders in relatives of early-onset probands was also observed (data not shown). Accordingly, ages of onset in affected relatives of affected probands might be downward biased by their being members of high-risk families.

We also observed another different but perhaps related birth-cohort effect (data not shown). There was a tendency for higher rates of SA disorder in later-born cohorts of relatives of SA probands. A similar trend was also observed for BP but not for UP, perhaps because later-born cohorts of relatives might have not yet passed the age at risk for UP.

Discussion

Studies on the rates of psychiatric illness in relatives of psychiatric and normal probands have consistently found the familial aggregation of certain disorders in the population. However, estimates of morbid risk in relatives vary considerably across studies, for many reasons, such as differences in procedures, in diagnostic criteria, or in populations, even leading to the question whether such estimates have any meaning at all. In the present study, we were more interested in comparisons of the relatives of various proband groups than true morbid risks, paying particular attention to the diagnostic material available for both the probands and their affected relatives.

The direction of our findings is similar to that generally reported by published studies on affective disorders. Depression aggregates in relatives of each proband group and bipolarity predominates in relatives of bipolar probands. The bipolar/non-bipolar distinction is even more pronounced in the present study, perhaps due to the rather long follow-up information which could have purified our UP proband sample. The relatively low rates of affective disorders in relatives compared with other studies, and the apparent relation between major and minor depression, can be explained in part by differences in the perception of episodes of affective disturbance in Sardinians, as already shown in other Mediterranean (Gershon et al. 1975) or rural (Coryell et al. 1981) areas. Likewise, cultural factors could also help to explain why men appear to have lower rates and later ages of onset of UP compared with women, as well as increased rates of alcoholism, drug abuse and personality disorders.

In our sample, SA probands seem to occupy an intermediate position between BP and UP probands from the viewpoint of the rates of major affective disorders in relatives, which is in agreement with the studies of Angst (1966), Angst et al. (1979a), Mendlewicz et al. (1980) and Baron et al. (1982). Gershon et al. (1982, 1988) found similar results in relatives of chronic SA probands, while probands with acute SA disorder showed the highest morbid risk for affective disorder in relatives. Tsuang et al. (1977, 1980), Rice et al. (1987) and Andreasen et al. (1987) found lower rates of major affective disorders in relatives of SA compared with BP and UP probands. The inconsistency across studies is attributable in part to variations in sampling and selection criteria and to population differences. In particular, samples recently collected in the United States show such high rates of UP in relatives of each proband group that differences are hardly observed if the rates of all affective disorders are combined in relatives. Subdivisions of both probands and affected relatives by polarity could provide more information, particularly if the assessment is longitudinal, since syndrome shifts in the long-term course are frequently observed, as reported for instance in SA patients (Marneros et al. 1988). Indeed, we found differences between SA-B and SA-D. In particular, there was a certain degree of homotypology in families with SA-B, while SA-D appeared to be more heterogeneous. Our data agree with those of Angst et al. (1979b), who found a higher risk for SA psychoses (the polarity in relatives was not specified) in the families of manic SA probands and a higher risk for neuroses in the families of non-manic SA probands. Other studies were not consistent with regard to the relevance of polarity in SA disorder. Possible explanations might be that the sample sizes were generally small, and the RDC dichotomy between manic and depressive SA subtypes was originally based on cross-sectional observations only.

With regard to schizophrenia, some studies reported an elevated incidence either in relatives of SA-D probands (Rice et al. 1987) or, using a different RDC subtyping, in relatives of probands with predominantly schizophrenic SA disorder (Baron et al. 1982). Other studies found an elevated incidence of schizophrenia in relatives of SA probands whatever the subtype, probably because their probands were selected among patients with a previous diagnosis of schizophrenia (Kendler et al. 1986) or were chronic SA (Gershon et al. 1988). We did not subtype SA probands according to the predominance of schizophrenic or affective features; however, the rates of chronic schizophrenia in relatives of both SA-B and SA-D probands were so low that an underinclusion of predominantly schizophrenic SA probands can be reasonably suspected in our outpatient sample.

The most peculiar finding in our study is that SA disorder with a bipolar course appears, to a certain degree, to breed true in families, which contrasts with the majority of previous studies. One possible explanation may be our perusal of records belonging to affected relatives, since, as underlined by Winokur (1984), psychotic symptoms are usually poorly detected using only direct interviews or information from other relatives. Indeed, studies based on either the family-history or the family-study method invariably found very few cases of relatives with SA disorder. The only exception was the report by Angst et al. (1979a) who, with an accurate use of record material, found 26 secondary cases of SA disorder out of 1004 first-degree relatives of SA probands. Nevertheless, they found more secondary cases of schizophrenia ($n = 46$) and unipolar depression ($n = 37$). On the other hand, some large pedigrees have been reported in which a "schizoaffective-like illness" apparently "breeds true" within the pedigree (Kaij 1967; Walinder 1972).

Whatever the reasons for the discrepancies in the literature, they reflect the different viewpoints regarding the nosology of SA disorder. According to the Kraepelinian dichotomy, SA disorder would be a rare condition representing the improbable genotypical coincidence of schizophrenia and affective disorder in one individual, as proposed for instance by Coryell and Zimmerman (1988). In contrast, according to the unitary model proposed by Crow (1986), there would be a continuum in the major

psychiatric disorders, with more cases characterized by both affective and schizophrenic symptoms compared with pure affective or pure schizophrenic cases. The latter possibility appears to be confirmed by the excess of SA probands in our sample, even though there might be an over-representation due to the nature of our centre. On the other hand, we cannot exclude peculiarities in cultural, environmental, or genetic factors in Sardinia leading to an excess of SA disorder and its apparent breeding true in families.

Our data can also fit the hypothesis of SA disorder as a separate nosological entity, more or less related to affective disorder. We found some similarities between SA and affective disorders, including the acceleration of onset in later-born cohorts of probands, increased risks in relatives of early-onset probands and in relatives belonging to younger birth cohorts. Birth-cohort effects have already been observed in affective disorders (Klerman et al. 1985; Rice et al. 1987; Gershon et al. 1987). They can be explained by a diathesis-stress paradigm with an increasing "stress" which appears to be shared by affective and SA disorders, whatever their genetic relationship.

Future work will explore genetic models of transmission, also extending the examination to more distant relatives. Larger sample sizes will also allow further subdivisions of patients, particularly SA, in order to test any heterogeneity, as suggested for instance by Maj (1989), or confirm and explain our preliminary observations of peculiar risks in certain genetic conditions which are typical of Sardinia (Bocchetta et al. 1989, 1990).

Acknowledgement. We thank Miss Maura Usai for valuable assistance in preparing the manuscript.

References

Andreasen NC, Rice J, Endicott J, Coryell W, Grove WM, Reich T (1987) Familial rates of affective disorder. Arch Gen Psychiatry 44:461–469

Angst J (1966) Zur Aetiologie und Nosologie endogener depressiver Psychosen. Springer, Berlin Heidelberg New York

Angst J, Felder W, Lohmeyer B (1979a) Schizoaffective disorders: results of a genetic investigation. I. J Affect Dis 1:139–153

Angst J, Felder W, Lohmeyer B (1979b) Are schizoaffective psychoses heterogeneous? Results of a genetic investigation. II. J Affect Dis 1:155–165

Baron M, Gruen R, Asnis L, Kane J (1982) Schizoaffective illness, schizophrenia and affective disorders: morbidity risk and genetic transmission. Acta Psychiatr Scand 65:253–262

Bocchetta A, Pedditzi M, Bernardi F, Corona R, Del Zompo M (1989) Thalassaemia minor and affective disorders. In: Stefanis CN, Soldatos CR, Rabavilas AD (eds) Psychiatry today, accomplishments and promises. VIII World Congress of Psychiatry Abstracts. Elsevier, Amsterdam, p 395

Bocchetta A, Del Zompo M, Corsini GU (1990) Glucose-6-phosphate dehydrogenase deficiency and psychoses. In: Cazzullo CL, Sacchetti E, Conte G, Invernizzi G, Vita A (eds) Plasticity and Morphology of the Central Nervous System: a Challenge for Psychiatry of the Nineties. Kluwer Academic Publisher, Dordrecht Boston London, pp 211–220

Breborowicz G, Trzebiatowska-Trzeciak O (1976) A method of testing differences in morbidity risk for affective psychoses. Acta Psychiatr Scand 54:353–358

Coryell W, Winokur G, Andreasen N (1981) The effect of case definition on affective disorder rates. Am J Psychiatry 138: 1106–1109

Coryell W, Zimmerman M (1988) The heritability of schizophrenia and schizoaffective disorder. Arch Gen Psychiatry 45:323–327

Crow TJ (1986) The continuum of psychosis and its application for the structure of the gene. Br J Psychiatry 149:419–429

Gershon ES, Mark A, Cohen M, Belizon N, Baron M, Knobe K (1975) Transmitted factors in the morbid risk of affective disorders: a controlled study. J Psychiatr Res 12:283–299

Gershon ES, Hamovit J, Guroff JJ, Dibble E, Leckman JF, Sceery W, Targum SD, Nurnberger JI Jr, Goldin LR, Bunney WE Jr (1982) A family study of schizoaffective, bipolar I, bipolar II, unipolar, and normal control probands. Arch Gen Psychiatry 39:1157–1167

Gershon ES, Hamovit JH, Guroff JJ, Nurnberger JI (1987) Birth-cohort changes in manic and depressive disorders in relatives of bipolar and schizoaffective patients. Arch Gen Psychiatry 44:314–319

Gershon ES, Delisi LE, Hamovit J, Nurnberger JI Jr, Maxwell ME, Schreiber J, Dauphinais K, Dingman CW, Guroff JJ (1988) A controlled family study of chronic psychoses. Arch Gen Psychiatry 45:328–336

Kaij L (1967) Atypical endogenous psychosis: report on a family. Br J Psychiatry 113:415–422

Kendler KS, Gruenberg AM, Tsuang MT (1986) A DSM-III family study of nonschizophrenic psychotic disorders. Am J Psychiatry 143:1098–1105

Klerman GL, Lavori PW, Rice J, Reich T, Endicott J, Andreasen NC, Keller MB, Hirschfield RMA (1985) Birth-cohort trends in rates of major depressive disorder among relatives of patients with affective disorder. Arch Gen Psychiatry 42:689–693

Maj M (1989) A family study of two subgroups of schizoaffective patients. Br J Psychiatry 154:640–643

Marneros A, Deister A, Rohde A (1988) Syndrome shift in the long-term course of schizoaffective disorders. Eur Arch Psychiatry Neurol Sci 238:97–104

Mendlewicz J, Linkowski P, Wilmotte J (1980) Relationship between schizoaffective illness and affective disorders or schizophrenia: morbidity risk and genetic transmission. J Affect Dis 2:289–302

Rice J, Reich T, Andreasen NC, Endicott J, Van Eerdewegh M, Fishman R, Hirschfield RMA, Klerman GL (1987) The familial transmission of bipolar illness. Arch Gen Psychiatry 44: 441–447

Tsuang MT, Dempsey GM, Dvoredsky A, Strauss A (1977) A family history study of schizoaffective disorder. Biol Psychiatry 12:331–338

Tsuang MT, Winokur G, Crowe RR (1980) Morbidity risks of schizophrenia and affective disorders among first-degree relatives of patients with schizophrenia, mania, depression and surgical conditions. Br J Psychiatry 137:497–504

Walinder J (1972) Recurrent familial psychosis of the schizoaffective type. Acta Psychiatr Scand 48:274–283

Winokur G (1984) Psychosis in bipolar and unipolar affective illness with special reference to schizo-affective disorder. Br J Psychiatry 145:236–242