Assortative Mating and Affective Disorders: Psychopathology in Offspring

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FAMILIAL aggregation has been frequently observed among probands with depression, anxiety disorders, and alcoholism (Gershon et al. 1976; Goodwin et al. 1973; Crowe et al. 1983). Because of the familial nature of these disorders, offspring of such probands have been identified to be at high risk for developing these illnesses themselves (Tarter 1983). Information regarding such risk has come from several sources: retrospective studies of patients with psychiatric disorders; studies of children whose parents are being treated for these disorders; and longitudinal follow-up studies of children with symptoms of the disorder.

Although most studies of high-risk children have been conducted with children of schizophrenic mothers, there is increasing evidence that children of parents with depression, alcoholism, and anxiety disorders are also at increased risk for psychopathology. Reviews of the studies of offspring of probands with major depression have shown high rates of symptomatology and impairment (Orvaschel et al. 1980; McKnew et al. 1979; Beardslee et al. 1983), with a prevalence of diagnosable illness ranging from 33% to 45%, most of it affective in nature. A family history of depression appears to be the major risk factor for depression in children. Negative environmental factors such as family discord, instability, and disruption are consistently reported both in retrospective studies of adult depressives and in studies of children with depression (Orvaschel et al. 1980).

Children of alcoholic parents have an even greater risk of suffering from the numerous disorders than has been reported for children of depressives. Infants born to mothers who drink heavily during pregnancy may develop fetal alcohol syndrome, which is characterized by physical, emotional, and intellectual deficits (Steinhausen et al. 1982).

Children of alcoholics have an approximately fourfold risk of developing alcoholism, with males at a much greater risk than females; the effects of paternal versus maternal alcoholism may differ as well (Cloninger et al. 1979). The unstable home environment in which these children are raised has likewise been well-documented as characterized by family disrup-

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tion, frequent divorce, and low socioeconomic status (Adler and Raphael 1983).

An association between childhood conduct disorder and adult alcoholism has been demonstrated in both retrospective studies of alcoholics and prospective studies of children with hyperactivity and conduct problems (Goodwin et al. 1975; Cadoret and Gath 1978; Alterman et al. 1982).

Although the risk of psychopathology in offspring of parents with anxiety disorders has not been established, studies of the relatives of adults with panic disorder, phobia, obsessive-compulsive disorder, and general anxiety disorder show an increased risk of anxiety disorder compared to normal populations (Crowe et al. 1983). However, the lack of specificity of transmission is notable for most of the disorders, with the exception of panic disorder and possibly obsessive-compulsive disorder. The diagnostic overlap both within the anxiety disorders and between anxiety disorders and affective disorders presents a major difficulty in interpreting family studies in this area. Weissman et al. (1984a,b) found that children under the age of 18 of parents with depression and agoraphobia or panic disorder had increased risk of separation anxiety, panic disorder, and phobic disorders, compared to children of parents with major depression only or normal controls. This finding has been confirmed in a more recent direct interview study of these children (Weissman et al. 1987).

Several studies have reported a link between childhood school refusal or separation anxiety and either phobic anxiety or panic disorder in adulthood (Berg et al. 1974; Gittelman-Klein 1975). In general, studies of the early history of agoraphobic adults report the onset of phobias prior to age 10 in a large proportion (Sheehan et al. 1981).

Although there is a consensus in the above studies that offspring of probands with the above-cited psychiatric disorders are at increased risk for psychopathology, there are few data regarding the mechanism for the elevated risk. Twin and cross-fostering studies have established the involvement of genetic factors in at least some subtypes of these disorders. Further, the negative home environments of these children are noted throughout, and all of the major psychiatric disorders are related to major and chronic disruption in the parental role. Bothwell and Weissman (1977) reported that social role impairment of depressed women persisted up to 4 years after cessation of the acute episode of depression. Impaired marital functioning of both depressed and alcoholic patients has been a consistent finding. Thus, it is likely that genetic predisposition is potentiated by the detrimental environment that is so often characteristic of parents with these disorders.

One phenomenon related to both familial disruption and elevated risk to offspring is concordance for psychiatric disorders in parents. The present study therefore focuses on the effects of parental concordance for psychiatric illness in general and alcoholism in particular.

Previous reports from our family study of 215 probands and their 459 offspring over the age of 6 have shown that when parents are concordant for alcoholism, children are more likely to become alcoholic themselves, and are also more likely to develop conduct disorder in childhood and antisocial personality in adulthood (Merikangas et al. 1985a,b). Similar findings emerged for depression and anxiety disorder. There was a linear relationship between number of parents ill and rates of depression and/or anxiety disorders in children (Weissman et al. 1984a,b). However, these data were considered preliminary because the children were not examined directly, but the information was obtained via family history from one or both parents.

METHODS

Probands

The analysis reported herein is based on 133 white probands with major depression defined according to modified Re-

search Diagnostic Criteria (RDC), who were in treatment at the Yale University Depression Research Unit or other facilities in the Department of Psychiatry. They were group matched by sex and age with 82 normal controls who had no history of psychiatric illness, and who were obtained from the 1975 community survey of Weissman and Myers (1978). Complete pedigrees for each proband were systematically obtained and diagnostic assessments according to RDC were made for every living or dead adult first-degree relative and spouse.

The depressed probands were classified according to the presence or absence of other diagnoses, such as alcoholism and anxiety disorders. The onset of alcoholism in all of the probands was chronologically secondary to major depression. All probands with primary alcoholism or antisocial personality were excluded from the study. Anxiety disorder included agoraphobia, panic disorder, or general anxiety disorder and could have occurred either concomitant to or temporally separate from depressive episodes.

Direct interviews were obtained from adult relatives and spouses whenever possible. If not, family history data were obtained from multiple informants and from medical records. Direct interviews were conducted with 40% of the sample, and family history information was available from multiple informants in over 55% of the relatives. Diagnostic assessments of the relatives were made blindly with respect to status of the proband, using a best estimate procedure (Leckman et al. 1982). Diagnoses of adult relatives and spouses were made according to modified RDC and were based upon all available information.

At the time of the original study, offspring under age 18 were not directly interviewed because diagnostic instruments and procedures for the assessment of psychiatric disorders in children were not available. A direct interview study of children was initiated 6 years after the original study had begun. All probands with offspring under age 18 at the time of the original proband interview were contacted and asked to be reinterviewed, and 87% of the eligible probands agreed to participate.

In order to determine the current clinical status and social functioning of the parents, each parent was interviewed separately by independent interviewers. A third interviewer interviewed a parent (preferably the mother) about the child, and at another time, the child about him/herself, in order to obtain a comprehensive assessment of the child's psychiatric, behavioral and social functioning. Parents were asked to complete self-administered reports about themselves and about each of their children, and children (approximately 10 years and over) were asked to complete self-administered reports about themselves. Authorized by both parent and child, we asked each child's teacher, pediatrician and, when indicated, other health care providers to complete questionnaires about the child. Direct interviews were obtained with 83% of the eligible children, and 97% of the children had a report from at least one parent. 84% of the mothers and 72% of the fathers also completed the diagnosit interviews about themselves.

The interviewers all had a minimum of 5 years' clinical experience with children and included two child psychologists, two child psychiatry fellows, and two masters-level school psychologists. They were blind to the diagnostic status of the parent for the child interviews and blind to the clinical status of both the child and the previous data on the parents for the interviews on current parent status.

Assessment of Children

Adapted for use in longitudinal studies as a reliable and valid instrument for obtaining lifetime diagnoses, the K-SADS-E (Puig-Antich 1982; Orvaschel et al. 1982; Chambers et al. 1985) with *DSM-III* addenda was used in our pilot study at the Yale Psychiatric Institute to assess diagnoses in the children. Findings suggest that interviewing a parent and child sepa-

rately and combining the results of the two interviews provides a more complete and accurate diagnostic assessment of the child. The K-SADS-E is the core of a comprehensive interview that we assembled to be administered to a parent about the child and to the child about him/herself. A more detailed description of the assessment procedures of the children is given by Weissman et al. (1987).

Best Estimate Diagnoses

A best estimate diagnostic procedure was employed in which a child psychiatrist and clinical psychologist who were not involved in the interviewing reviewed all sources of information and independently assigned a diagnosis. Discrepancies were resolved by a third source, who also independently and blindly reviewed all available information. We plan to reinterview all offspring and parents in 2 years. The initial level of agreement was 83%. Major depression in the offspring was defined according to modified RDC criteria as in our adult sample, with four major symptoms, 4 weeks duration with impairment or one week duration plus incapacitation/hospitalization.

RESULTS

There were a total of 215 probands in the original study, of whom 165 had offspring. Of these, 239 adult offspring were assessed in the original study with the SADS-L and Family History RDC, and 220 offspring ages 6–23 were assessed in the high-risk component of the study with the Kiddie-SADS-E, for a total of 459 offspring for whom diagnostic assessments were completed.

The age and sex distribution of the offspring is shown in Table 1. There were approximately equal numbers of males and females, and most of the offspring were between the ages of 18 and 24. A substantial proportion of the offspring were well into adulthood. The number of children per family did not differ between the two proband groups.

Table 1

NUMBER OF OFFSPRING BY AGE AND SEX

	Male	*Female*	*Total*
High-Risk Study			
< 12 years	20	15	35
12–17 years	39	53	92
18–24 years	46	47	93
Family Study			
18–24 years	58	52	110
≥ 25 years	65	64	129
TOTAL	228	231	459

The rates/100 of diagnoses among the offspring by the original proband groups consisting of probands with major depression and normal controls is shown in Table 2. There was a twofold risk of major depression in the offspring of depressed compared to normal parents. Any anxiety disorders and any psychiatric diagnosis were also significantly higher among offspring of the depressed probands. Rates of alcoholism and conduct disorder or antisocial personality were not significantly higher among the offspring of the depressed compared to the normal probands.

Because a large proportion of the spouses of both the depressed and normal probands also had psychiatric diagnoses and because of the large number of secondary diagnoses in the probands, disorders in the offspring were also examined according to the diagnoses of both parents, rather than by the original case-control design. Thus, normal control probands with spouses with psychiatric illness were reclassified by the diagnosis of their spouses. Table 3 shows the number of parents ill, by diagnosis. These diagnostic groupings are not mutually exclusive. That is, in all of the couples in which both members were affected, at least one parent had major depression. From Table 3, it can be seen that concordance for major depression, anxiety disorders, and any diagnosis was fairly common, whereas concordance for alcoholism was not. This could be attributed to the

Table 2

RATES/100 OF DIAGNOSES IN OFFSPRING BY PROBAND GROUP

Diagnosis in Offspring	*Proband Parent*		
	Depressed (N=273)		*Normal* (N=186)
	(Rates/100)		
Major Depression	23.4	**	11.3
Alcoholism	7.7		8.6
Conduct/Antisocial	15.8		10.7
Anxiety Disorder	34.8	**	22.6
Any Diagnosis	67.8	**	52.2

**=$p<.01$.

sampling of probands with major depression, in which primary alcoholism was an exclusion criterion.

Table 4 presents the rates of major depression and any RDC diagnosis among the first-degree relatives of the spouses of the depressed probands. This analysis shows that the relatives of the spouses with major depression had significantly higher rates of major depression and any RDC diagnosis than the relatives of the spouses who did not have major depression. Similarly, the relatives of the spouses with any RDC diagnosis also had a significantly increased risk of any RDC diagnosis compared to the relatives of the spouses who did not meet RDC for any lifetime diagnosis. This suggests that there was familial aggregation of major depression and psychiatric illness in general in the families of the spouses who had major depression and those with any diagnosis. For these results, one can conclude that it is likely that the concordance for major depression between the probands and their spouses can be attributed to assortative mating for depression or some related trait rather than to marital interaction resulting in the onset of depression in the spouse of the depressed proband.

Table 5 shows the relationship of any psychiatric illness in parents to disorders in offspring. The strongest linear trend was observed for any diagnosis in offspring. That is, when neither parent was affected, one-third of the children had a diagnosis; when one parent was ill, over half of the children had a diagnosis; and when both parents were affected, three-quarters of their offspring had a diagnosable psychiatric illness.

Major depression, anxiety disorders, and antisocial personality/conduct disorder also showed significant linear trends according to the number of parents with

Table 3

NUMBER OF PARENTS ILL, BY DIAGNOSIS

Diagnosis in Parents	*% of Proband Couples* (N=165 Couples)		
	Both	One	Neither
Major Depression	15.7	50.9	33.3
Alcoholism	4.8	14.5	80.6
Anxiety	10.3	44.2	45.5
Any Diagnosis	41.2	38.2	20.6

Table 4

RATES/100 OF PSYCHIATRIC DISORDERS AMONG PARENTS AND SIBLINGS OF SPOUSES OF PROBANDS WITH MAJOR DEPRESSION

Spouse	*Rates/100 Among Relatives of Spouses*	
	Major Depression	Any RDC Diagnosis
Major Depression		
Present	4.8*	25.5*
Absent	1.4	16.7
Any RDC Diagnosis		
Present	3.0	23.4***
Absent	1.3	12.3

*=$p < .05$.
***=$p < .001$.

any RDC diagnosis. Alcoholism was the only diagnostic category among children that was not related to parental concordance for any diagnosis.

Table 6 shows the effects of parental concordance for alcoholism. There is a strong linear trend in the relationship of rates of alcoholism among offspring and number of parents with alcoholism. Offspring have a twofold risk of alcoholism when one parent has alcoholism compared to offspring of couples in which neither parent has alcoholism. Offspring of couples concordant for alcoholism have a threefold increase in risk compared to those in which one parent is affected.

Similarly, for antisocial personality and conduct disorder, there is a strong significant linear trend according to the number of parents with alcoholism. Rates of major depression and anxiety disorders are not significantly increased among offspring of alcoholic parents.

The effects of parental concordance for alcoholism and any RDC diagnosis on diagnoses in offspring are summarized in Table 7. The strongest effect of parental assortative mating was seen for alcoholism, in which offspring had a threefold increase in risk of alcoholism compared to offspring of couples in which only one member had alcoholism. Nearly 50% of the offspring over age 18 of the couples concordant for alcoholism had alcoholism

Table 5

RATES/100 DIAGNOSES IN OFFSPRING BY NUMBER OF PARENTS WITH ANY PSYCHIATRIC DIAGNOSIS

Diagnosis in Offspring (Rates/100)	*Any Illness in Parents*			
	Both (N=201)	*One* (N=173)	*Neither* (N=85)	*Chi Square*[a]
Major Depression	29.4	23.7	14.1	7.38**
Alcoholism	8.0	8.1	8.2	0.01
Antisocial/Conduct	17.4	14.5	3.5	8.51**
Anxiety	41.8	23.7	14.1	25.99***
Any Diagnosis	75.1	57.8	36.5	39.05***

[a]Linear trend in proportions, 1 *df*.
**=$p < .01$.
***=$p < .001$.

Table 6

RATES/100 DIAGNOSES IN OFFSPRING BY NUMBER OF PARENTS WITH ALCOHOLISM

Diagnosis in Offspring (Rates/100)	*Any Illness in Parents*			*Chi Square*[a]
	Both (N=25)	*One* (N=84)	*Neither* (N=350)	
Major Depression	28.0	17.9	13.0	.80
Alcoholism	32.0	10.7	5.7	18.77**
Antisocial/Conduct	36.0	21.4	10.3	18.07**
Anxiety	44.0	32.1	28.3	2.67
Any Diagnosis	80.0	69.1	58.3	7.16*

[a]Linear trend in proportions. 1 *df*.
*=$p<.05$.
**=$p<.01$.

themselves, compared to 11% when neither parent had alcoholism. The effect of assortative mating for alcoholism was also seen in the increased risk of antisocial personality in the offspring over age 18, where 30% had antisocial personality, compared to 2% of the offspring of couples without alcoholism. There was a 1.7-fold increase in the risk of conduct disorder in the younger offspring and of antisocial personality in the older offspring of parents who were concordant for alcoholism.

Lastly, parental concordance for any diagnosis was related to extremely high rates of diagnoses in offspring, with an average of 70–80% being affected. Concordance for any diagnosis in parents was related to a 1.8-fold increase in risk of anxiety disorders, and a 1.3-fold increase in risk of any diagnosis in offspring compared to that of offspring with one parent ill.

DISCUSSION

The results indicate that parental concordance for psychiatric illness in general and alcoholism in particular are related to an increased risk of psychiatric disorders in the offspring. The findings from our earlier studies, in which the information on children was derived from family history rather than direct interviews, were confirmed in these analyses. The effects of parental concordance for major depression and anxiety disorders will be presented elsewhere.

Also consistent with earlier studies was

Table 7

SUMMARY OF EFFECTS OF PARENTS' CONCORDANCE FOR ALCOHOLISM AND ANY RDC DIAGNOSIS ON DIAGNOSES IN OFFSPRING (N=456)

Concordance in parents	*Diagnosis with Increased Risk in Offspring*	*Relative Risk (Both vs. One Parent With Diagnosis)*
Alcoholism	Alcoholism	3.0
	Conduct Disorder or Antisocial Personality	1.7
Any Diagnosis	Anxiety Disorders	1.8
	Any Diagnosis	1.3

a high degree of concordance for psychiatric illness among the parents, with 41% of 41% of the couples both manifesting a diagnosable psychiatric illness (Merikangas 1982). Concordance between spouses for a disorder does not necessarily imply that assortative mating for that trait occurred. Such concordance could result from convergence for the trait as a result of marital interaction. However, evidence regarding aggregation of the trait among first-degree relatives of the spouse with the trait, who do not share the environment with the proband, would exclude the latter explanation. In our data, it was concluded that assortative mating had occurred because increased rates of psychopathology were observed among the relatives of the ill spouses compared to those of the well spouses.

Concordance for a trait may also result from mate selection for another factor that may be a correlate or precursor to the trait on which concordance is assessed. Indeed, differential mate selection among persons with affective disorders is unlikely, because the onset of these disorders in both spouses generally occurs several years after the time of marriage. We have previously suggested that mate selection in these couples may be related to personality factors that are premorbid to affective disorders or to similar levels of social differentiation (Merikangas and Spiker 1984).

These data clearly demonstrate that offspring of concordant parents are at significantly increased risk of developing psychopathology. We have also demonstrated some degree of specificity of transmission of the effects of assortative mating as well, with children exhibiting a tendency to develop the same disorders as those which are manifest in their parents. Such specificity may be attributable to shared liability, modeling of parental behavior, or a combination thereof.

Evidence for continuity between childhood and adulthood manifestation of similar syndromes was provided by the remarkably similar increase in the relative risk of disorders among the younger and older offspring of couples in particular mating classes. For example, similar elevations of risk were observed for conduct disorder among younger offspring and antisocial personality among adult offspring of dual-mated alcoholic couples, compared to those of other parental mating types. In contrast, little continuity was observed between conduct disorder and antisocial personality among the younger and older offspring of parental mating for depression alone.

Although assortative mating among parents has been shown to be an important risk factor for the development of psychopathology in their children, mechanism by which this increased risk occurs is not known. It is likely that assortative mating is related to both increased genetic risk and a clustering of environmental risk factors. Couples with concordance for affective disorders have been found to have significantly worse marital and social adjustment, and an elevated divorce rate, when compared to couples in which only one member is affected (Merikangas et al. 1983; Merikangas 1984).

The implications of these findings in terms of primary prevention, the ultimate aim of high-risk studies, are not clear. Genetic counseling of prospective couples in which both have a family history of depression, anxiety disorders, or alcoholism is an unlikely intervention. However, efforts toward secondary intervention depend upon the specification of risk factors with which to intervene. Our study and those of others have identified the presence of parental concordance for depression, alcoholism, and other disorders as one such factor related to significantly increased risk in children. Efforts at identification of such situations by routine assessment of the spouse of patients who come for treatment, and application of interventions that attempt to minimize the marital and parental role impairment, may help to decrease the substantially elevated rates of disorders in the children examined in this study.

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