Incidence of Psychiatric Disorder in Offspring at High and Low Risk for Depression

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Abstract. First onsets (incidence) of suicide attempts and *DSM-III* psychiatric disorders, including major depression, any anxiety disorder, conduct disorder, or substance abuse were determined in a 2-year longitudinal study of 174 offspring at high and low risk for major depression. All of the suicide attempts, the first onsets of major depression, and anxiety disorders were in offspring of depressed parents. Compared with asymptomatic offspring, offspring with subclinical manifestations of major depression, conduct disorder, and substance abuse at the initial interview were significantly more likely to become incident cases of the same disorder over the next 2 years. Either conduct disorder or substance abuse at initial interview were highly predictive of first onset of each other, but not of any other disorders 2 years later. Family risk factors (such as poor marital adjustment, parent-child discord, low cohesion, and affectionless control) at initial interview were associated with increased incidence of substance abuse, or conduct disorder, but not major depression or anxiety disorder. Combining both retrospective and prospective data, the overall suicide attempt rate was 7.8% in the offspring of depressed parents as compared with 1.4% in the offspring of nondepressed parents. By age 20, over 50% of the offspring of depressed patients reported a major depression. *J. Am. Acad. Child Adolesc. Psychiatry,* 1992, 31, 3:640–648. **Key Words:** depression, suicide.

It is a basic tenet of chronic disease epidemiology that studies examining the association between any disorder and a potential risk factor require a longitudinal design where risk factors are first measured in persons free of the disorder who are then followed longitudinally. Persons who develop first onset of the disorder (incidence cases) are compared with those who don't develop the disorder on the presence or absence of the antecedent risk factor. This comparison is the approach used in the longitudinal Framingham Heart Study that demonstrated the association between serum cholesterol levels and cardiovascular disease and, more recently, between body weight fluctuations and mortality (Lissner et al., 1991).

In psychiatry, data on risk factors established through study of incidence cases are rare. Most studies cross-sectionally examine correlates of prevalent cases. This approach is useful for identifying potential risk factors. However, prevalent cases (i.e., new and existing cases at any one time) compound the incidence (first occurrence) of a disorder with its duration, recurrence, and recovery patterns. Prevalent cases are often either recurrent cases of past episodes or chronic cases of current episodes. Although the factors that predict relapse or recovery may be quite different from those that predict first onset, misleading results about presumed risk factors may be obtained from prevalence data (Warner et al., unpublished). This situation for psychiatric disorders is characteristic of most chronic diseases, such as cardiovascular disease, cancer, etc.

Previously, we have shown cross-sectionally that offspring of parents with a history of major depression are themselves at increased risk for psychopathology. In particular, offspring with one or more depressed parent as compared with neither parent depressed were found to have higher lifetime rates of major depression and anxiety disorder (Weissman et al., 1987). In addition, we have cross-sectionally assessed the relative importance of several family risk factors, including the parents' psychiatric diagnosis as predictors of psychopathology in offspring (Fendrich et al., 1990b). We found that the offspring of depressed parents were exposed to more of the family risk factors. Parental diagnosis of major depression was more important than family risk factors in predicting major depression or anxiety disorder in the offspring of depressed parents, but were associated with depression in the offspring of nondepressed parents. Family risk factors, however, did predict conduct disorder in offspring, regardless of parental diagnoses. These findings suggested that there was a varying impact of family risk factors by parental and by offspring diagnoses.

This present study extends our previous research by examining incident cases of the major *DSM-III* (American Psychiatric Association, 1980) psychiatric disorder in offspring followed over 2 years. More specifically, we determine: (1) whether offspring of depressed, as compared to nondepressed, parents have an increased risk for suicide attempts and first onset of psychiatric disorders over a 2-year period, and (2) whether the risk factors identified in our cross-

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sectional prevalence study show the same pattern of association with incident cases in the offspring.

Methods

Sample

Offspring were selected for the study by virtue of the presence of a lifetime history of major depression (as defined by the Research Diagnostic Criteria) in their parents. A complete description of the probands (parents) and their assessment has been published elsewhere (Weissman et al., 1982). The depressed probands had received treatment at the Yale University Depression Research Unit. The normal controls came from a 1975 community survey conducted in New Haven and had no history of psychiatric illness based on at least four direct interviews (the last two using Schedule for Affective Disorders and Schizophrenia-Lifetime Criteria [SADS-L] and Research Diagnostic Criteria) during an 8-year period. All probands were white and group-matched by age and sex. Previous reports from this study have compared 125 offspring of 56 depressed proband parents with 95 children of 35 nondepressed proband parents. In psychiatric assessments of probands and their spouses taken at the time of the study, however, three control probands and six spouses of control probands reported a lifetime history of major depressive disorder; the depressed parents from these nine families had 28 offspring. Thus, the sample consists of 220 from 91 families who were between the ages of 6 and 23 at initial interview (time 1), with 153 offspring from 65 families and with one or more depressed parents, and 67 offspring from 26 families with neither parent depressed. Diagnostic information from parents and/or offspring is available on all 220 offspring at time 1.

Two years after the initial interview, all 91 families were contacted for a second interview (time 2). Eighty-five (93%) of the 91 families with a total of 203 offspring consented to participate at time 2. The present study on the course of major depression consists of 174 offspring (79% of the total sample) about whom diagnostic information was obtained from direct interview (using the K-SADS-E, see below) with offspring and/or parents at time 2. More detailed information about time 2 interviews have been provided elsewhere (Fendrich et al., 1990a). The 174 offspring included in the present study and the 46 who did not participate did not vary significantly by age, sex, or their parents' diagnoses.

The age and sex distribution of the sample of 174 offspring included in these analyses did not vary by the parent's diagnosis. Over two-thirds of the sample were offspring of one or more depressed parent ($N = 121$; 69.5%); less than one-third of the sample ($N = 53$; 30.5%) were offspring of parents without a history of major depression. There were 95 girls (54.6%) and 79 boys (45.4%). Twenty-eight offspring (16.1%) were under 12 years of age, 76 (43.7%) were between 12 and 18 years of age, and 70 (40.2%) were 19 to 23 years of age at initial interview. The offspring were approximately 2 years older at follow-up.

Diagnostic Assessment of Offspring

A modified version of the Schedule for Affective Disorders and Schizophrenia for School-Aged Children, Epidemiologic Version (K-SADS-E) formed the core of a comprehensive interview administered to the parent about the offspring and to the offspring about him or herself. Interviewers were blind to the parent's diagnostic status. The K-SADS-E used in this study was modified to generate most of the major *DSM-III* psychiatric disorders. In these analyses, we employ five *DSM-III* diagnostic groups, including major depression, any anxiety disorder (i.e., including separation anxiety, panic disorder, phobia, obsessive-compulsive disorder, and overanxious disorder), any conduct disorder, any substance abuse (including alcohol and drug abuse), and dysthymia.

Best Estimate Diagnosis

Diagnoses of offspring were based on the Best Estimate procedure (Leckman et al., 1982). To derive Best Estimate diagnoses, a clinical psychologist and child psychiatrist who were not involved in the interviewing, independently and blind to the diagnostic status of the parent, reviewed all sources of information and assigned a lifetime *DSM-III* diagnosis for each offspring. Discrepancies in diagnoses by these independent evaluators were resolved by a third source, who also independently and blindly reviewed all available information. In a previous report we show that the interrater reliability between two psychiatrists for the offspring diagnoses was excellent for the major psychiatric disorders (Weissman et al., 1988).

Definition of Incidence

An incident case for a particular disorder is defined as no evidence of a current or lifetime diagnosis at time 1 and a first onset of a specific diagnosis in the interim noted at time 2 interview. In deriving incidence rates for a specific disorder, all cases identified at time 1 are eliminated from the denominator.

Time 1 Predictors of Incidence

Parental depression. Exposure to one or more depressed parent (as previously defined) as compared with neither parent depressed was examined as a predictor of incidence in offspring.

Number of parental depressive episodes. The maximum of the mother's and father's Best Estimate number of major depressive episodes was used as a measure of the magnitude of the exposure of the offspring to the parents' depressive illness. The score was trichotomized into 0, 1, or 2 or more episodes, because of the small number of parents experiencing more than two episodes. For most of the analysis, only the comparison of the effect of being exposed to two or more episodes as compared to one episode was used.

Age and sex of offspring. Age was dichotomized at age 16 in some analyses, and in other analyses, age was used as a covariate and treated as a continuous measure. Male offspring and female offspring were compared to see if incidence varied by sex of offspring.

Socioeconomic status. A five-point scale based on the Hollingshead two-factor index of social position was used to measure socioeconomic status of the family (Hollingshead,

1965). Families in upper and middle social classes (social classes I, II, III) were compared with families of lower social class (i.e., IV, V).

Subclinical symptoms. Offspring with symptoms not meeting definite *DSM-III* criteria because of insufficient number of symptoms or duration at time 1 were considered to be subclinical and were compared with those offspring with no symptoms of depression at time 1 as a predictor of an incident case in the follow-up period.

Offspring Social Functioning and Impairment

Children's Global Assessment Scale (C-GAS) (Shaffer et al., 1983). The C-GAS was designed to measure overall functioning in the offspring. Scores range in value from 1 to 100 (the highest functioning). Based on the epidemiologic studies, a cut-off of 71 was used as a dichotomized score (Bird et al., 1987). The C-GAS score was based on the child psychiatrist's Best Estimate at time 1.

Family risk factors. Parents and offspring completed a battery of self-report measures at both times that were used to construct family risk factors. Their conceptualization and scoring is described elsewhere (Fendrich et al., 1990a). The family risk factors selected include: (1) an index of poor marital adjustment based on parent reports on the Short Marital Adjustment Test (Locke and Wallace, 1956); (2) divorce based on parents' reports of marital history; (3) parent-child discord based on mother's reports on a family life events questionnaire; (4) "affectionless control" based on the caring and overprotection subscale of the Parental Bonding Instrument (Parker et al., 1979); and (5) "low cohesion" based on the cohesion subscale of the Family Adaptability and Cohesion Evaluation Scale (Olson et al., 1979). The association between the presence of these risk factors at the initial interview and incident cases over the 2 years was assessed.

Epidemiologic catchment area study (ECA). For comparison, age and sex adjusted 1-year incidence rates of psychiatric disorders comparable with those used in the offspring were calculated from the ECA, a community-based survey. Only data from the New Haven site of the ECA where most of the offspring lived were used. (See Robins and Regier, 1990, for description of ECA.) Analysis of incidence data included persons interviewed initially and at 1-year follow-up. Excluded from the denominator in the calculation of incidence for each disorder were persons with a missing value for a diagnosis at initial interview.

Statistical Analysis

Chi-square statistics were used initially to test the association between incidence and predictor variables for categorical data. In addition, predictors were looked at simultaneously in a maximum likelihood logistic regression, using the SAS Logist procedure (SAS Institute, Inc., 1986). The antilogarithm of the regression coefficient for predictor yields an odds ratio for evaluation of the impact of the predictor. The cumulative probability (i.e., the probability of onset of the psychiatric disorder during anytime between birth and the given age interval) was estimated by the Kaplan-Meir method (Kalbfleisch, 1980). Equality of survival distributions for different groups was tested by means of the log rank test for homogeneity, which weights larger survival times more heavily, and the Wilcoxin test, which places more weight on the early survival times.

Results

Suicidal Behavior over 2-Year Period

There were no completed suicides over the 2-year period. Two reports of first suicide attempts occurred in the offspring of depressed patients over the 2 years. One was a 20-year-old male who took three "pain" pills during a depressive episode and then went to an emergency room. He was admitted to the psychiatric service for 3 days and discharged to outpatient treatment. The second was a 10-year-old boy who tried to strangle himself with a belt and was saved by his brother. The mother was unaware of the episode and did not report it at interview. In addition, two episodes of suicide attempts occurring before time 1 were reported that had not been reported previously.

Taking both reports at time 1 and 2 over the lifetime, 12 (7.8%) offspring of depressed parents had made at least one suicide attempt or gesture, whereas one (1.4%) offspring of nondepressed parents made a suicide attempt.

Overall 2-Year Incidence Rates

The first and second columns of Table 1 compare incidence rates in the offspring by parental diagnosis. All 10 incident cases of major depression and all eight of anxiety disorder were in offspring of depressed parents. Within the high-risk group, the 2-year incidence rate of major depression was 13.2%, and for anxiety disorder it was 11.3%. Rates of conduct disorder, although higher for offspring of depressed parents by parent diagnoses, did not reach statistical significance (14.0% versus 8.3%). Incidence rates of substance abuse were nearly equal across groups. Not shown here, the incidence rates in the offspring for any of these disorders did not vary by their age, sex, or family social class with one exception. Six of the seven incident cases of substance abuse ($p < 0.10$) were in offspring who were 16 years or older at the time of the initial interview.

The third column of Table 1 lists the distribution of first onset diagnoses in all offspring over the 2-year follow-up. Relatively high 2-year incidence rates were observed for all of the specific disorders. ranging from 4.5% for substance abuse disorder to 12.1% for conduct disorder.

The fourth column lists the 1-year incidence rates/100 from the New Haven site of the ECA, where most of the offspring and families lived, and includes only subjects ages 18 to 23, the youngest age in the ECA study. Considering the time period and age difference, the incidence rates are overall somewhat comparable. The lower rate of substance abuse in the offspring sample, as compared with the ECA ages 18 to 23, is undoubtedly the result of the younger age of the offspring.

Subclinical Symptoms, Diagnosis, and Impairment at Time 1

Table 2 examines 2-year incidence rates by the presence

TABLE 1. *Two-Year Incidence Rate/100 of DSM-III Diagnosis in Offspring by Parent Diagnosis*

Time 2 *DSM-III* Diagnosis in Offspring	Two-Year Incidence Rate/100 (No. of cases)						One-Year Incidence Rate/100 (No. of cases)
	One or More Parent Depressed		Neither Parent Depressed		Total		ECA New Haven Site (Ages 18–23)
	N	%	*N*	%	*N*	%	
Major depression	(10)	13.2	(0)	0.0*	(10)	8.5	(15) 7.2
Any anxiety disorder	(8)	11.3	(0)	0.0*	(8)	7.0	(11) 5.4
Separation anxiety	(5)	5.1	(0)	0.0			
Overanxious disorder	(5)	4.5	(1)	1.9			
Phobia	(6)	6.0	(0)	0.0			
Substance abuse	(5)	4.8	(2)	4.0	(7)	4.5	(14) 9.2
Alcohol	(5)	4.8	(2)	4.0			
Drug abuse	(3)	2.6	(0)	0.0			
Conduct disorder	(13)	14.0	(4)	8.3	(17)	12.1	Not available

*$p < 0.05$.

or absence of subclinical symptoms of the same disorder and by the presence of other psychiatric disorders and impairment at time 1 for the full sample of offspring. Subclinical symptoms at time 1 for any disorders, except anxiety, predicted the onset of the specific disorder by time 2, 2 years later. Offspring with subclinical symptoms of major depression had an incidence rate nearly six times that of asymptomatic offspring at time 1 (33.3% versus 5.7%; $p = 0.010$, Fisher's exact test); offspring with subclinical symptoms of substance abuse disorder at time 1 had an incidence rate of over ten times that of asymptomatic offspring (22.2% vs. 2.2%; $p = 0.003$, Fisher's exact test), and offspring with subclinical symptoms of conduct disorder at time 1 had an incidence rate over eight times that of asymptomatic offspring (66.7% versus 8.3%; $p < 0.001$, Fisher's exact test).

The presence of major depression, dysthymia, or anxiety disorder in offspring at time 1 did not predict incidence of other psychiatric disorders by time 2. However, substance abuse at time 1 predicted incidence of conduct disorder by time 2. Alternatively, conduct disorder at time 1 predicted incidence of substance abuse by time 2. Impairment (i.e., CGAS score <71) at time 1 also predicted incidence of conduct disorder by time 2.

Family Risk Factors

Table 3 demonstrates that the offspring of depressed as compared with nondepressed parents were significantly more exposed to most of the family risk factors, including affectionless control, parental divorce, poor marital adjustment, and low family cohesion.

Table 4 compares the 2-year incidence rates of various diagnoses in offspring by presence or absence of five family risk factors at time 1. Because of the low numbers, we cannot stratify by parental diagnosis or examine these risk factors simultaneously. Incidence of major depression or any anxiety disorder between time 1 and 2 was not associated with the presence of family risk factors at time 1. The incidence of substance abuse in offspring was associated with parental divorce and affectionless control of parent at time 1. There were no parental divorces over the 2-year period noted and all had occurred before time 1. The incidence of conduct disorder in offspring was associated with affectionless control, low family cohesion, and presence of any risk factors at time 1. Offspring from families reporting divorce ever, as compared with offspring without divorce in the family, had seven times the risk for developing substance abuse disorder (10.4% versus 1.9%; $p = 0.03$, Fisher's exact test). Compared with other offspring, offspring from families reporting affectionless control had over four times the risk for developing conduct disorder (26.5% versus 5.9%; $p < 0.01$, Fisher's exact test).

Cumulative Incidence or Probability

Figures 1 to 4 combine the information from the times 1 and 2 longitudinal assessment of offspring and show the cumulative probability of developing major depression, anxiety disorder, conduct disorder, or substance abuse in offspring by parental diagnoses during any time between birth to age 20. The numbers were too small between ages 20 to 25 to consider.

These figures clearly show the increase of these four types of disorders in the offspring of depressed parents. By age 20, over 50% of the offspring of depressed parents reported a major depression. There are no cases of major depression before age 10 in the offspring of nondepressed parents. The rates of major depression increased markedly after puberty in both groups and increased at a greater rate in the offspring of depressed parents.

The patterns are different for anxiety disorders. There is a steep increase in rates of anxiety in the offspring of depressed parents from early childhood (age 5) that increases linearly until age 20. In the offspring of nondepressed parents, the rates plateau at a low level at age 10. For conduct disorder, the rates in both groups began to increase around age 10, but remain higher in offspring of depressed parents. The rates of substance abuse do not begin to increase until adolescence but remain higher in the offspring of depressed parents.

Discussion

Suicide attempts and first onsets of major *DSM-III* psychiatric disorders, including major depression, any anxiety dis-

TABLE 2. *Two-Year Incidence Rate/100 of Disorder in Offspring (N = 174) by Presence or Absence of Subclinical Diagnosis, Other Psychiatric Diagnosis, or Impairment in Offspring by Time I*

Presence (Yes) or Absence (No) of Factor in Offspring at Time 1	Two-Year Incidence Rates/100 in Offspring			
	Major Depression	Any Anxiety	Substance Abuse	Conduct Disorder
Subclinical symptoms of the same disorder				
No	5.7	6.1	2.2	8.3
Yes	33.3**	8.2	22.2**	66.7***
Major depression				
No	—	7.8	5.4	10.6
Yes	—	3.8	2.3	16.2
Dysthymia				
No	8.3	7.1	4.5	10.0
Yes	11.1	5.9	4.5	23.8
Anxiety				
No	6.7	—	5.8	11.5
Yes	13.8	—	2.0	13.3
Substance abuse				
No	8.9	7.7	—	10.4*
Yes	0.0	0.0	—	42.9
Conduct disorder				
No	5.8	7.3	1.5***	—
Yes	28.6+	5.3	23.8	—
C-GAS				
<71 (Impaired)	4.8	7.0	3.0	20.3***
71+	17.5	6.9	5.7	3.0

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

order, conduct disorder, or substance abuse were examined in a 2-year longitudinal study of 174 offspring at high and low risk for major depression. All of the suicide attempts and gestures and new onsets of major depression and anxiety disorders over 2 years were in offspring of depressed parents. Compared with asymptomatic offspring, offspring with subclinical manifestations of major depression, conduct disorder, and substance abuse disorder at the initial interview were significantly more likely to become incident cases of the specific disorder. The presence of either conduct disorder or substance abuse at initial interview predicted a first onset of the other disorder at 2-year follow-up. Impairment in functioning at initial interview predicted conduct disorder by follow-up. Family risk factors were associated with elevated incidence of substance abuse disorder and conduct disorder, but not major depression or anxiety disorder in the offspring.

TABLE 3. *Exposure of Offspring to Family Risk Factors by Parent Diagnosis*

Family Risk Factors at Time 1	One or More Parents Depressed		Neither Parent Depressed	
	N	%	*N*	%
Affectionless control	34	34.3	11	21.1****
Parent-child discord	34	28.1	12	22.6
Parental divorce	48	39.6	7	13.2**
Poor marital adjustment	64	67.3	11	23.4***
Low family cohesion	59	59.6	20	38.4*

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.10$.

Because all of the incident cases in these later two disorders occurred in the offspring of depressed parents, it was not possible to determine the relative contribution of parental diagnoses and family risk factors for these disorders.

Limitations

The obvious limitations of this study point to several areas of needed research. Although while this is the largest published offspring study of depressed parents and also one of the few with a longitudinal design, a sample of 174 offspring with a broad age range is still small for examining incidence and for making predictions. Because of the sample size, we could not examine the impact of family risk factors in association with one another or their differential impact on incidence in offspring by parental diagnosis. Our follow-up period was only 2 years. Only the Hammen et al. (1990) high-risk study had a longer period (3 years). Finally, our list of family risk factors. although representative of those usually considered associated with child psychopathology, was not exhaustive.

Comparison with Other Incidence Studies

Comparisons with findings from other incidence studies are limited because of their rarity in psychiatry. Three studies of children could be found that purported to present incidence data. However, their data cannot be interpreted directly as such. The Albert and Beck study (1975) used a symptom scale (the Beck Depression Scale) and not a diagnostic measure. In a sample of 63 7th and 8th graders, they found that 33.3% had moderate to severe depression

TABLE 4. *Two-Year Incidence Rate/100 of* DSM-III *Psychiatric Disorder in Offspring by Presence or Absence of Family Risk Factor at Time I*

Absence (No) or Presence (Yes) of Risk Factor at Time I	Two-Year Rate/100 in Offspring (No. of Cases)							
	Major Depression		Any Anxiety		Substance Abuse		Conduct Disorder	
	N	%	*N*	%	*N*	%	*N*	%
Poor marital adjustment in parent								
No	(4)	8.5	(3)	6.4	(2)	3.1	(3)	5.0
Yes	(4)	7.4	(3)	6.7	(2)	3.2	(9)	14.5
Parental divorce ever								
No	(6)	7.1	(6)	8.0	(2)	1.9**	(10)	9.8
Yes	(4)	12.1	(2)	5.0	(5)	10.4	(7)	18.0
Parent-child discord								
No	(9)	10.1	(8)	9.1	(5)	4.3	(11)	9.9
Yes	(1)	3.5	(0)	0.0	(2)	5.3	(6)	20.0
Affectionless control								
No	(4)	5.6	(5)	7.0	(2)	2.1*	(5)	5.7**
Yes	(3)	11.1	(1)	3.7	(4)	11.1	(9)	28.1
Low family cohesion								
No	(4)	7.4	(1)	2.3	(1)	1.5	(3)	4.3****
Yes	(3)	6.7	(5)	9.3	(5)	7.8	(11)	19.6
Any risk factor above								
No	(2)	9.1	(1)	4.8	(0)	0.0	(0)	0.0
Yes	(8)	8.3	(7)	7.4	(7)	5.4	(17)	14.9*

*$p < 0.05$, **$p < 0.01$, ****$p < 0.10$.

symptoms. It is unclear if these were new (incidence) or new and existing (prevalence) cases. The same issue is raised in Kashani and Simmonds' report (1979) of 103 children ages 7 to 12 years from a family practice cohort born in one medical center. Whereas they reported an incidence rate of 1.9% for major depression according to *DSM-III*, it was unclear from the clinical reports of the two cases if these were new onsets or prevalent cases. Von Knorring et al. (1987), using a case registry of treated cases of the total population of Sweden, studied one cohort from birth to age 24 years. Applying *DSM-III* criteria to the hospital case records, they found a cumulative incidence in females of 3.2% for affective disorders, 4.6% for anxiety disorders, and 1.8% substance abuse, and in males, 1.1%, 4.7%, and 2.0%, respectively. Their lower incidence rates are probably the result of their inclusion of only hospital-treated cases. Thus, the less severe nonhospitalized cases were not included.

Hammen et al.'s unique study (1990) of 92 offspring of parents with major depression, bipolar illness, medical illness, or normals followed at 6-month intervals over 3 years provides the best comparison. The lifetime incidence presented as cumulative for major depression up to age 19 years in offspring by proband mothers' diagnoses was 67%, 33%, 45%, and 12%, respectively. Our cumulative incidence of major depression up to age 19 was about 52% in offspring of depressed parents and 28% in the offspring of nondepressed parents (Fig. 1). Our higher rates of major depression in offspring of nondepressed parents (28% as compared

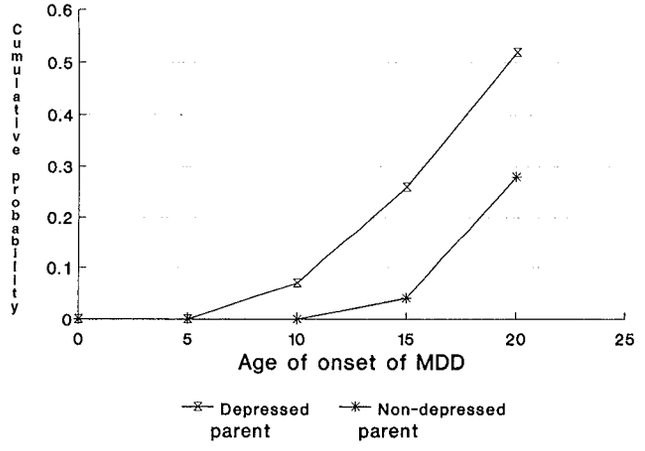

FIG. 1. Cumulative probability of major depression in offspring by parental major depression.

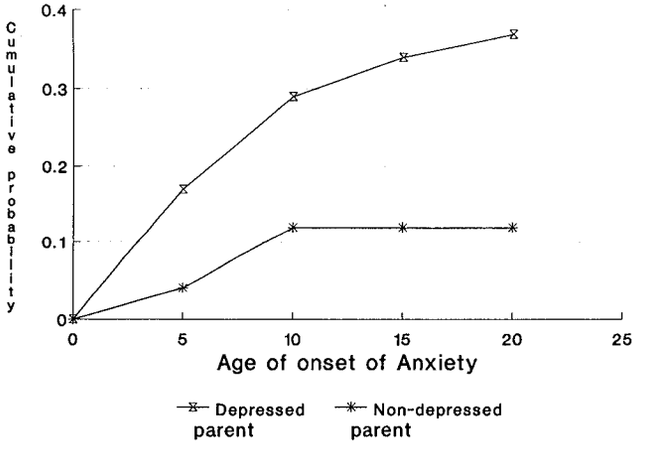

FIG. 2. Cumulative probability of anxiety disorder in offspring by parental major depression.

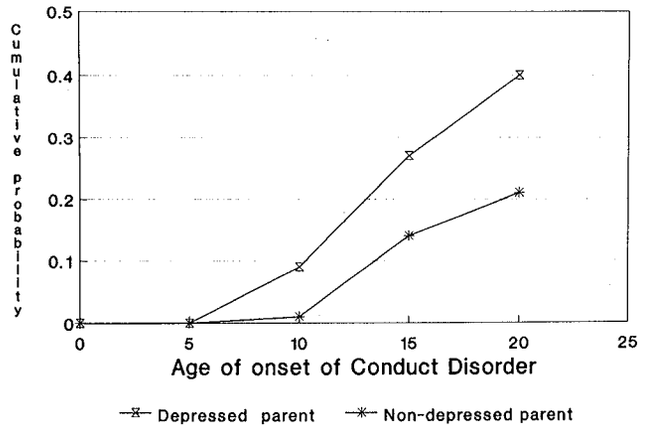

FIG. 3. Cumulative probability of conduct disorder in offspring by parental major depression.

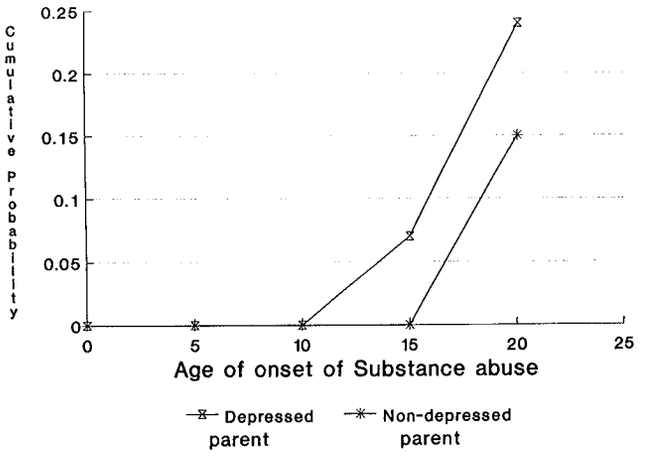

FIG. 4. Cumulative probability of substance abuse in offspring by parental major depression.

with 12% in the Hammen et al. study) may be due to presence of other nondepressive illness in our parents. Hammen et al. did not report cumulative probabilities for other disorders, probably because of their small sample.

Our findings, along with Hammen et al. (1990) suggest that over 50% of offspring of depressed parents will have experienced a major depression before age 20. Both studies also found a relative rarity of prepubertal onset major depression and increasing frequency at puberty, particularly in the offspring of depressed parents. The pattern for anxiety disorder was different and did not show the sharp increase at puberty in offspring of nondepressed parents.

The actual incidence data in the Hammen et al. (1990) study were not presented separately but are summed as internalizing (depression, anxiety) or externalizing (conduct disorder, substance abuse) disorders. However, some extrapolation can be made from the figures presented on lifetime diagnosis. For conduct disorder, by age 19, 32% of the offspring of depressed parents, 14% of medically ill parents, and 8% of normals were affected in the Hammen et al. study. Our rates for conduct disorder were 40% for offspring of depressed parents and 20% for offspring of nondepressed (Fig. 3). In the Hammen et al. study, the figures for separation anxiety disorder by age 19 were 18%, 7%, and 8% whereas ours, not shown, were 23% and 11%.

Kovacs et al. (1988, 1989), in a prospective study of 104 treated depressed children ages 8 to 18, calculated the cumulative probability of first onset of anxiety disorder up to age 18. The cumulative probability (using Kaplan-Meier estimates) by age 18 was 47% with a cluster of onsets between ages 9 and 11 years—earlier than onsets of major depression. By age 18, 38% of our offspring of depressed parents and 11% of nondepressed parents had developed an anxiety disorder (Fig. 2). We also saw a marked rise in anxiety disorders around age 10 in the offspring of depressed parents. Our findings in this later group are comparable to the Kovacs et al. findings. However, she has not reported rates in offspring by parental diagnosis.

Kovacs et al. (1988) found that 36% of her depressed children had developed conduct disorder by age 19, with the most frequent age of onset between ages 11 and 14. We found that about 40% of our offspring of depressed parents had developed conduct disorder by age 19, and 20% in the offspring where neither parent was depressed. We also found a sharp increase after about 10 years which plateaued at age 20. Again, our cumulative rates in the offspring of depressed parents were quite similar to Kovacs' treated children.

Incidence studies of psychiatric disorders in adults, while including larger samples, have limited comparability. Henderson et al. (1981) and Schwab et al. (1979) used symptom scales, and Hagnell et al. (1982) used ICD. Comparisons with the 1-year incidence rates found in the young adult population (18 to 23 years) of the New Haven site, where most of our offspring lived, are of interest. The 2-year incidence rate for major depressive disorder in this study was 8.5%, and the 1-year incidence rate in the New Haven ECA for adults ages 18 to 23 years was 7.2%.

The association between conduct disorder and alcoholism seen in our offspring is consistent with our findings on the transmission of these disorders between adults and children. In a separate family history analysis in which there was a partial overlap with these offspring, the rates of alcoholism and conduct disorder were increased about three-fold among offspring under 18 of parents with secondary alcoholism and major depression as compared with offspring of parents with major depression alone. For the adult offspring of these parents, there was a five-fold increased risk of antisocial disorder. Although risk of anti-social personality or conduct disorder was significantly increased among offspring of probands with major depression only, as compared to offspring of normal controls, the risk was far greater among offspring of parents with secondary alcoholism (Merikangas et al., 1985).

Importance of Subclinical Diagnosis

It is well recognized that chronic diseases have an insidious onset with a long latent period of mild symptoms before the emergence of the full syndrome. Our data were consistent with this point of view in that subclinical symptoms of depression, substance abuse, and conduct disorder were the

strongest predictors for first onset of the same disorder. Moreover, there was specificity in the prediction in that subclinical symptoms of one disorder did not predict another disorder with the exception of the reciprocal prediction of substance abuse and conduct disorder.

These findings on subclinical disorders as predictors of first onset cases are similar to those found in adult studies. Murphy et al. (1988, 1989), in a 16-year follow-up study of a community sample, found that premonitory symptoms were the strongest predictors of onset of major depression. Over the 16-year follow-up, subjects with prodromal symptoms at baseline were three times more likely to become incident cases. The ECA study also found that depressive symptoms not meeting criteria for major depression were among the single most important predictors of first onset major depression over 1 year. Persons with depressive symptoms at time 1 were over four times as likely to develop a first onset of major depression 1 year later (Horwath et al., unpublished).

The patterns of incidence for conduct disorder and substance abuse contrast with patterns exhibited by major depression and anxiety disorder. Incidence of conduct disorder and substance abuse were not associated with parental depression. On the other hand, incidence of conduct disorder consistently shows a strong association with family risk factors. These two disorders—conduct disorder and substance abuse—may be a consequence of the immediate family environment. Nevertheless, exposure to depressed parents may itself constitute an environmental risk to the offspring (Fendrich et al., 1990a). Furthermore, our study did not measure environmental stresses experienced in early childhood, before onset of subclinical symptomatology. More detailed observation and measurement of early childhood experiences are needed before their etiological importance can be ruled out.

Family Risk Factors, Conduct Disorder, and Substance Abuse

The prospective findings on the stronger association between family risk factors, parental divorce, affectionless control, and low family cohesion in parents, and conduct disorder in offspring parallel our cross-sectional findings where the strongest association between family risk factors (i.e., divorce, low family cohesion, parent-child discord) was found with conduct disorder in offspring and not the other disorders in offspring. These findings held even when parental diagnoses were added to the model (Fendrich et al., 1990a). Because of the low numbers in a prospective design, we could not stratify by parental diagnosis. However, the strong association we found between conduct disorder and substance abuse, with one of the disorders predicting the other, and the association of both with family risk factors (divorce and affectionless control) suggest that similar mechanisms may be operating in both disorders.

In our cross-sectional analysis, these same family risk factors were associated with onset of major depression in the offspring of nondepressed parents only. In this prospective study, all the incidence cases of depression and anxiety were in the offspring of depressed parents. Thus, the absence of an association of family risk factors with depression or anxiety in offspring may be the result of the absence of incidence cases of depression or anxiety in offspring of nondepressed parents. Considerably larger samples of offspring followed longitudinally are needed to examine these associations.

In summary, the prospective data confirm the high rate of first onset of psychiatric disorder in the young sample. The longitudinal findings also replicate our cross-sectional observation of the higher rates of depression, anxiety, and suicide attempts in the offspring of depressed parents. Our findings also highlight the paucity of longitudinal epidemiological and clinical data on younger populations, a fact well summarized in a recent Institute of Medicine report.

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