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Longitudinal Study of Diagnoses in Children of Women With Unipolar and Bipolar Affective Disorder

Constance Hammen, PhD; Dorli Burge, PhD; Elizabeth Burney, MS; Cheri Adrian, PhD

• School-age children of unipolar depressed, bipolar, chronically medically ill, or normal women were diagnosed every 6 months for up to 3 years. Offspring of unipolar women had the highest rates of disorder at all evaluations, but children of bipolar and medically ill mothers also experienced significant rates of disorder. Observing diagnoses from both past lifetime and prospective follow-up assessments, it appeared that most children who had diagnoses had onsets in preadolescence and continued a chronic or intermittent course of disorder. Thus, risk to offspring of ill mothers is not transitory and indicates a pernicious course that commonly includes affective disorders alone or in combination with behavior and anxiety disorders. (Arch Gen Psychiatry. 1990;47:1112-1117)

Numerous studies have documented children's risk for psychiatric symptoms and maladaptive outcomes if they have a parent with major affective disorder. Although elevated rates of dysfunction occur consistently, there is considerable variability in the quality of the methods and in conclusions about the nature and specificity of children's disorders as a function of parental illness.

One of the greatest gaps in the research on offspring of parents with affective disorder concerns the stability of children's psychiatric symptoms over time. Many studies have not differentiated between the acute effects and the ongoing consequences of parental illness. Longitudinal analyses are needed to provide a more reliable sampling of children's symptoms over the course of parental illness and to address issues of consistency of symptoms over time. Two studies have reported such longitudinal information. Nurnberger et al1 diagnosed 15- to 25-year-old offspring of bipolar families in a 1- to 2-year follow-up, and Billings and Moos2 had unipolar parents complete questionnaires about their children 1 year after an initial contact. We now report longitudinal follow-up diagnoses of children for up to 3 years after initial evaluation.

Additional gaps in the studies of children of parents with affective disorder are addressed. For instance, many of the earlier studies did not distinguish between parental unipolar and bipolar disorder, or used indirect methods of evaluating children's outcomes.3,14 Relatively few studies have employed comparison groups sufficient to test hypotheses about the specificity of parental affective illness, including, for example, nonaffective psychiatric controls or medically ill controls. The exceptions7,15,16 have tended to draw different conclusions, leaving open the issue of whether affective disorders are such, or illness generally, contribute to children's maladaptive outcomes. Only a few studies have directly compared children of unipolar and bipolar parents. Winters et al17 and Conners et al18 found greater dysfunction or symptoms associated with offspring of unipolar parents. On the other hand, Greenhill and Shopsin19 found that bipolar parents reported more symptoms in their offspring than did unipolar parents, and Radke-Yarrow et al20 found more severe attachment problems in the infants of bipolar than unipolar parents.

Only a handful of studies include direct interviews of children and their parents, which permit the fullest possible range of information for making DSM-III diagnoses of children. Several studies of offspring of unipolar21,22 and bipolar parents23,24,25 vary widely in the gender distribution of the parents and in the ages of the children. Not surprisingly, rates of diagnoses in children vary considerably, although most of the studies show elevated rates of lifetime disorder.

The present study includes school-age and adolescent children of mothers with unipolar or bipolar disorder, compared with chronically medically ill and normal women, who were followed up at regular intervals for up to 3 years, using direct interviews of both mother and child. The rates of lifetime diagnoses of children in the sample were previously reported.

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SUBJECTS AND METHODS

Sample

Ninety-two children participated in the investigation of offspring of women with major affective disorders, women with chronic medical illness, and normal controls. (Ninety-six were originally included, but four children of two women with chronic medical illness were excluded from the current analyses, as noted below.) At the time of recruitment into the study, children were between ages 8 and 16 years. No more than two children per family were studied directly, and when more than two were available, the youngest and oldest in the age range were selected. For 66% of the families, this meant that all children were studied. (Information about the diagnostic status of additional children, as reported by the mother, was noted previously.)

Table 1 gives the sex and age of the children by group. Overall, there were no differences by sex ($\chi^2[3]=1, n=92$). The groups differed somewhat in age ($F[3,88]=3.41, P<.05$), owing to younger girls in the groups with unipolar and normal mothers compared with all other groups.

The women with affective disorders were recruited from inpatient facilities, outpatient clinics, and private referrals. To capture chronic rather than acute effects, families were initially evaluated no sooner than 3 months after the mother's hospital discharge or admission to outpatient treatment. Only women who had multiple episodes of major depression were included in the unipolar sample, again to highlight chronic effects. Most of the women had been hospitalized at least once, indicating not just chronic but severe disorder. Insulin-dependent diabetes was selected as the chronic medical illness that would generally parallel the course of affective disorders in terms of chronicity as well as acute exacerbations sometimes requiring hospitalization. Two cases of severe early-onset rheumatoid arthritis were also included for similar reasons. Several of the medically ill women had experienced brief depressive adjustment reactions. Two medically ill women who had recurrent depressive episodes were excluded from the present analyses, and all the remaining women were psychiatrically normal. For all of the psychiatrically and medically ill women, the onset of their disorders had to have occurred before the child's birth or during his or her infancy. Normal women were recruited from the same or demographically comparable schools as the families in the other groups. Only those reporting no psychiatric history or treatment were included.

Demographic and Clinical Characteristics of Maternal Groups

The groups were primarily white (11 unipolar families [69%], 13 bipolar families [93%], 12 medically ill families [100%], and 17 normal families [71%]) but included black and Hispanic families in all groups except the medically ill. The racial distribution was not statistically different across groups ($\chi^2[3]=7.05, n=66, P>.10$). The women did not differ in age (mean ± SD), 38.3 ± 4.79 years. Significantly fewer unipolar (four [25%]) and bipolar (five [43%]) women were currently married, compared with medically ill (16 [67%]) and normal (16 [75%]) women ($\chi^2[1]=11.17, n=66, P=.01$). The groups did not differ in socioeconomic status according to Hollingshead ratings, except for the unipolar group, in which socioeconomic status was lower than the other groups owing to more women receiving public assistance because of psychiatric disability. However, the groups were comparable in educational level, with most having at least a high school education and some college or technical training. The majority of women in all the groups were in the middle and upper-middle socioeconomic categories.

The unipolar women had been hospitalized an average of 1.88 ± 2.2 times for psychiatric reasons and reported an average of 11.4 ± 8.3 lifetime episodes of major depression (and an additional six women said they had “too many to count”). Their mean age at onset of depression was 18.2 ± 7.8 years. Their Beck Depression Inventory (BDI) mean score at the initial evaluation was 20.4 ± 11.8. Women with bipolar disorders had been hospitalized a mean of 2.75 ± 2.3 times, with 7.2 ± 5.4 lifetime episodes (with one woman reporting too many to count) and a mean age at onset of 20.9 ± 8.8 years. Eight of the bipolar women could be classified as having bipolar I illness, the other four as having bipolar II. The initial mean BDI score for bipolar women was 15.9 ± 16.7. The medically ill women had been hospitalized for their medical problem a mean of 5.8 ± 8.6 times and had a mean age at onset of 17.4 ± 11.1 years. Their mean BDI score was 7.3 ± 6.1. The initial mean BDI score for normal women was 4.4 ± 3.8.

Procedure

Initial Evaluation.—The mother was seen for an interview session alone to complete a confirmatory diagnostic evaluation based on the Schedule for Affective Disorders and Schizophrenia, Lifetime version (SADS-L), and to provide information about her functioning and that of family members. Two to 4 weeks later, the mother and her child or children were seen for additional interviews, including the children's version of the SADS (Kiddie-SADS, or K-SADS), administered to both mother and child. Children also completed a variety of social-cognitive measures, and the mother and each child participated in interaction tasks that were videotaped and systematically scored for content and quality of communication. All these procedures are reported in detail elsewhere.

Follow-up Procedures.—At 6-month intervals, the mother and each child were interviewed for their symptom functioning since the previous contact. Mothers' diagnoses were based on the SADS, and the mother and each child were interviewed with the K-SADS separately. The majority of these follow-ups were conducted by telephone since it would have been impossible to retain families if they had to travel to UCLA from widely spaced areas of Southern California. Also, practical realities made it impossible for staff members to schedule visits to their homes. One study has suggested that the reliability of diagnostic information conducted by telephone is adequate, and our experience confirms this observation, as discussed below. Interviewers were advanced clinical psychology graduate students with special interests in child psychopathology and affective disorders and extensive training with the K-SADS. Reliability for face-to-face interview diagnoses, established on the basis of a subsample of 35 children independently rated by a second judge, yielded a coefficient of $k=.84 (P<.001)$. Initially, the interviewer was “blind” to the mother's diagnostic status, but often information from the mother or child revealed her clinical status. In most cases, the same interviewer contacted both mother and child, to obtain the fullest possible discussion of symptoms.

Diagnostic Decisions.—Children's diagnoses were based on data supplied by mother and child independently. In some cases, additional diagnostic information was available from treating therapists. The research team, consisting of the senior researcher (a clinical psychologist) and advanced clinical psychology graduate students, reached consensus diagnoses by consensus. All available information, including reports of school performance, family and peer functioning, as well as reports from a therapist, if available, was drawn on to make final diagnostic decisions. Such information clarified symptoms and degree of impairment. When the child and the mother provided discrepant information, the research team discussed the issues and generally gave weight to whoever reported information on existing symptoms. For example, the literature suggests that children report more depression than their parents report. In some cases the child also reported more sensitive information about substance use or antisocial conduct than the parent may have been aware of, and this information was given preference in diagnostic decisions.
Timing of Episodes.—Efforts were made to obtain exact dates of onset of children's episodes from the mother. When the mother was unable to recall exact dates, she was asked to specify the week or month of onset. Interviewers facilitated children's recall by inquiring how symptoms related to important school events or holidays. When neither mother nor child could specify time of symptom onset or described an intermittent pattern, symptoms were dated from the beginning of the follow-up period, or in the case of the initial evaluation, from January 1 of the year in which symptoms emerged.

Attrition.—In the unipolar group, 16 families entered the study, and 11 (69%) of 16 completed all 3 years, with 100% (22 children) finishing 1 year and 14 (88%) of 16 families (20 children) completing 2 years. Of the five families that were incomplete, two withdrew, one was unavailable for follow-up, and two entered the study late and were still continuing at the time of the present analyses.

The bipolar sample started with 14 families, with six families (seven children) completing 3 years. Twelve (86%) families finished 1 year, and nine (64%) (11 children) completed 2 years. Of the eight families that did not complete the follow-up, two withdrew, five were unavailable (moved or unable to be contacted), and one entered late and is continuing.

In the medical group, nine (75%) of 12 families completed all 3 years, with 100% (14 children) staying for 1 year and 10 (83%) families with 11 children staying for 2 years. Two families withdrew, and one moved out of the area. Twenty-four normal group families began the study, and 11 (46%) (11 children) completed 2 years. Of the eight families that did not complete the follow-up, two withdrew, five were unavailable, one moved, and one withdrew.

Of the children in the groups with unipolar or bipolar mothers who did not complete all of the follow-ups, the proportions who had a diagnosis or not were similar to the proportions in their groups overall. There were no differences between completers and dropouts in age or sex. Thus, there did not seem to be a selection bias in the study, and 21 (88%) with 34 children completed all 3 years, with 22 (92%) families (35 children) completing 1 year and 21 (88%) with 34 children staying 2 years. Of the three families not continuing, one was unavailable, one moved, and one withdrew.

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RESULTS

Lifet ime Diagnoses by Group

Children's definite diagnoses, based on interviews covering past and current disorders and including all follow-up contacts, were tabulated. Table 2 gives the types of diagnoses by maternal group. It is apparent that the children of unipolar mothers were highly likely to have obtained at least one diagnosis (82%), compared with the children of medically ill and normal mothers (48% and 38%, respectively). The offspring of bipolar mothers also had high rates of diagnoses (72%) but somewhat less than the children of unipolar mothers. It might also be noted that in general the children of bipolar mothers had somewhat milder disorders than did the children of unipolar mothers, with rates of minor depression and anxiety disorders that elevated their overall rates of diagnosis.

Lifet ime Incidence of Major Depression

As Table 2 indicates, depressive disorders were the most common diagnoses and most evident in the children with unipolar mothers. Nearly half of all cases of major depressive episode occurred in the children of unipolar mothers (10 of 22 cases). Table 3 gives the survival curve estimates of age at onset of major depression. The figures confirm the relative rarity of childhood onset but indicate increasing frequency of onset from about the age of 12 years. The log-rank test of the survival curves indicates significant differences among the maternal diagnostic groups ($\chi^2 = 11.72, P = .0087$), reflecting the increased incidence in the children of unipolar mothers compared with the children of bipolar and medically ill mothers, who were similar, and the children of normal mothers, who had very low rates of major depression.

Diagnostic Status During Follow-up Observations

It is particularly instructive to examine the children's diagnostic status during the follow-ups, since the evaluations, occurring every 6 months up to a total of 3 years, might be expected to yield the most accurate and complete picture of their adjustment. Table 4 gives the diagnoses during the follow-ups for children who completed at least 1 year of evaluation, according to whether the child had a new disorder, relapse, or chronic disorder. Two striking features are apparent. The children of bipolar mothers and comparison group children had relatively few chronic, recurrent, or new disorders during the follow-up.
ill children was quite low during the follow-ups, with one each in the groups with medically ill and normal mothers.

**Effects of Gender and Age**

Analyses of age at onset of first major disorder as a function of the child's gender indicated relatively similar rates for boys and girls through about age 14 years. Boys had a cumulative probability of disorder of .41, compared with girls' probability of .39. In the age interval of 15 to 19 years, however, boys' cumulative probability (.41) was exceeded by that of girls (.69). However, the overall Kaplan-Meier survival curve estimates did not differ significantly (log-rank test, $\chi^2(1) = 0.06, P = .81$). In terms of prevalence of disorders observed during the follow-up interviews, girls and boys were generally similar in rates and were approximately equally represented in the different types of disorders. For instance, of 11 children with major depression observed during follow-ups, six were girls and five were boys.

**Comorbidity**

As Table 2 indicates, not only did children of mothers with affective disorders have high rates of definite diagnoses, they also tended to have multiple diagnoses, averaging 2.6 in the children of unipolar mothers, a rate higher than in any other group.

It was relatively rare for children to display only a single type of symptom. For instance, in the year-1 follow-up, counting only definite diagnoses (and excluding minor depression), only a few youngsters displayed affective disorders alone: three with unipolar mothers, one with a bipolar mother, one with a medically ill mother, and none with normal mothers. Even fewer showed only externalizing disorders such as conduct disorder or substance use disorders, and a few displayed only anxiety disorders. By contrast, the more typical pattern was for a mixture of affective and nonaffective disorders. There were six such children in the group with unipolar mothers in year 1, displaying major depression and/or dysthymic disorder along with conduct disorder and/or substance use disorder.

Viewing the sample available for all 3 years of the follow-up, children were classified as showing internalizing disorders only (affective and/or anxiety disorders) vs “other” disorders (presence of externalizing disorders such as conduct disorder, substance use, and attention deficit, with or without concurrent emotional disorders). Taken as proportions of children who had diagnosable disorders, internalizing patterns appeared in 58% of the children of unipolar mothers, 80% of the children of bipolar mothers, 25% of the children of medically ill mothers, and 70% of the children of normal mothers. These proportions were not significantly different across groups of children with diagnoses ($\chi^2(8) = 15.12$, $n = 95, P > .10$).

**COMMENT**

To our knowledge, this is the first report of a direct-interview longitudinal follow-up of children at risk for psychopathologic conditions owing to maternal unipolar depression. Along with that of Nurnberger and colleagues, this is also the first such follow-up of children of bipolar parents. The present study confirms the conclusion of the earlier cross-sectional research: having a mother with a major affective disorder is associated with considerable risk for diagnosable disorder in the child. Despite the relatively small sample sizes of the current groups, the effects were strong and consistent.

The children of unipolar mothers fared especially poorly. They showed the highest overall likelihood of diagnoses. Fully half of this group had some form of affective disorder at some point, including major depression or dysthymic disorder. Of the 22 in this group, five had at least one recurrence of a major depression that had occurred before the study. One child with severe depression during the follow-up committed suicide. One child had possible cyclothymia over a 2-year period, and in one child hypomania developed, along with major depression, leading to treatment for bipolar disorder. (There was no apparent history of bipolar disorder in the family, but the possibility that a relative had been misdiagnosed must be entertained.) The offspring of unipolar moth-
ers also had the highest group rates of conduct disorder and substance use disorder, which mostly continued over the entire course of the follow-up.

The children of bipolar mothers also had high rates of symptoms but generally lower rates of definite diagnoses than did the children of unipolar mothers. Rates of diagnosis do not accurately reflect the severity of the disorders, which we believed to be unequivocally worse among children of unipolar mothers. Four of the 15 children of bipolar mothers had definite affective disorders (depression) over the course of the study. In one child possible hypomanic episodes developed, and one appeared to have a cyclothymic pattern, but these symptoms were at levels that did not meet criteria for definite diagnoses. The bipolar sample of Nurnberger et al omitted offspring from the longitudinal phase if they already displayed psychopathologic changes, and their offspring were older (between 15 and 25 years old). They found that in five of 58 subjects major affective disorders developed over a 1- to 2-year period. In our sample of offspring of bipolar mothers, the presence of anxiety symptoms was especially noteworthy, including both diagnosable and nondiagnosable forms of overanxious disorder and separation anxiety. Recent cross-sectional studies generally have reported similar rates of anxiety disorders and depressive disorders in bipolar samples. We found rates of conduct disorder to be lower than those reported in other direct-interview studies, but substance use disorders, which we observed to be at subsyndromal levels in children of bipolar mothers, appeared to be roughly similar.

Comparing children of unipolar and bipolar mothers, we speculate that the risk to the latter group is somewhat milder in terms of impairing disorders that occur at young ages. This observation is in accord with previous direct comparisons by Conners et al and Winters et al, who found fewer differences between offspring of bipolar and normal mothers. However, the studies that did find severe disease in offspring of bipolar mothers have studied them at later ages, including adulthood. Others have noted the appearance of mild and subsyndromal affective disorders and hyperthymic or dysthymic styles. Although the offspring of bipolar mothers appear to function better than their counterparts with unipolar mothers in terms of diagnoses and severity of disorders, it is likely that continuing follow-up of these youngsters would reveal later onsets of significant disorder; as other clinical research has suggested. Nevertheless, the early appearance of significant, developmentally disruptive disorders in the offspring of unipolar mothers bodes ill for their future adaptive functioning.

The presence of concurrent disorders has been commonly noted in research on childhood depression in general and in offspring studies more specifically. The current results affirm the relative rarity of finding depressive disorders alone. Common patterns include depression with other disorders, such as anxiety reactions, or combinations of depression with externalizing disorders, such as conduct and substance use disorders.

In general, age and sex differences were not salient in the diagnoses; neither were there differences between offspring groups in sex and age patterns. However, more detailed analyses of symptom patterns related to developmental differences might identify important differences and ought to be pursued in larger samples of children.

Few children had new onsets of disorders during the follow-up. The most common pattern among children with diagnoses was for relatively chronic or intermittent courses of the same disorder. Other investigators, studying children of mixed groups of psychiatrically ill parents or depressed children in treatment, have also observed persisting symptoms. Most of the disorders that we observed made their initial appearance before adolescence. The pattern of relative stability of disorders over time is, of course, an especially malignant one for children who must master a variety of coping and adaptational skills during their school-age years. Impairment of functioning academically and socially might be expected to contribute to low self-esteem and vulnerability to further depression in youngsters and possibly greater susceptibility to depression in adulthood.

The present study addresses the issue of specificity of maternal affective disorders for negative outcomes. Like Hirsch et al but unlike Klein et al and others, we found that the rates of disorder for children of medically ill mothers were elevated, although not as high as those of the children of unipolar mothers. Possibly, the different findings can be attributed to medical groups that may or may not include individuals with depressive reactions, or that may differ in severity of disorder. We have argued elsewhere for the presence of three overlapping but independent factors contributing to children's outcomes: severity of disorder, chronic stressful conditions that may be confounded with disorder, and current depressed mood that may be independent of diagnosis. In statistical analyses aimed at separating the three factors, we found that current depressed mood and chronic stress contributed more to children's negative outcomes than did maternal psychiatric diagnosis itself.

Our findings regarding the specificity issue therefore suggest that children's disordered functioning is not unique to parental affective disorders as such. Indeed, a variety of "high-risk" studies of children concur with the observation that parental psychiatric disease is likely only one of several risk factors that account for generally poor outcomes for children of various kinds of patients. Although the likely impact of genetically transmitted dysfunction should not be minimized, the search for the psychosocial contributors to children's risk should be intensified. It is apparent from offspring research, both cross-sectional and longitudinal, that when a parent is ill, the children are likely also to display disturbance. Thus, affective disorders are not just individual illnesses; they are also family illnesses that may have lifelong consequences.

This study is limited in a number of ways. The sample is small and precluded more detailed investigation of the patterns of particular disorders in children. Children might be at risk by virtue of not only maternal diagnoses but paternal diagnoses as well. There is evidence of assortative mating in women with affective disturbances. Also, the present unipolar sample included patients with relatively severe and chronic depression, and larger samples of more diverse patients will help to clarify the relationship between variations and subtypes of depression and children's risk for disorder. A related issue, the relationship of coexisting disorders in the mother to children's diagnoses, is also important. The problems of attrition also plague any longitudinal study. Our rate of compliance was actually high; nevertheless, relatively more bipolar families were unavailable for follow-up. Finally, our diagnoses of children during the follow-ups relied on telephone interviews and interviewers who were not blind to maternal diagnostic status. Both of these strategies were aimed at retaining the sample by having contact with the same interviewer over time. On balance, we believe that the information obtained is valid and reliable and certainly does not overreport events that did not occur. Masked interviewers would be virtually impossible, in our experience, owing to the information divulged by mothers and children. In any case, improvements in assessment and sample retention would be welcome in future studies.

Despite limitations, this study's strengths include inclusion of both unipolar and bipolar subjects, as well as a medically ill
comparison group, and follow-ups for up to 3 years by highly trained interviewers. The results unambiguously attest to the risk for children of ill mothers for severe and often continuing disorder. Our next goal is to help clarify the processes that contribute to the risk.

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