Depression and Anxiety Disorders in Parents and Children

Results From the Yale Family Study

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• **The children (aged 6 to 17 years) of probands with primary major depression, with and without various anxiety disorders, were compared with the children of a matched normal control group. The results from the study of these young children parallel our previous findings among the adult first-degree relatives of these probands. Depression in the proband increased the risk of depression in the children. Depression plus panic disorder or agoraphobia in the proband conferred an additional risk of depression and of an anxiety disorder in the children. Panic disorder in the parents conferred more than a threefold increased risk of separation anxiety in the children. Other factors that increased the risk to children were degree of familial loading for psychiatric illness, parental assortative mating, and parental recurrent depression. The findings suggest a relationship between depression and some of the anxiety disorders, and between adult panic disorder and agoraphobia and transmission of anxiety disorders to children.**

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In a previous report we showed that depression plus anxiety disorder in the probands increased the risk of depression and of anxiety disorders in their adult first-degree relatives.[1] When the specific anxiety disorders (agoraphobia, panic, general anxiety) in the depressed probands were examined, we found that depression plus panic conferred a high risk of depression and anxiety in the relatives. The first-degree relatives of probands with major depression plus panic were at increased risk for major depression, panic, phobia, and/or alcoholism. The comparison groups for the study included the relatives of probands with major depression alone and the relatives of a matched normal control proband group. These findings were based exclusively on data from adult first-degree relatives, aged 18 years and older.

Extending the study of the adult relatives of probands with depression and anxiety disorders, we examined the risk of psychiatric disorder in the children (aged 6 to 17 years) of those probands with both major depression and specific anxiety disorders. The purpose was to learn about the relationship between the adult and childhood depression and anxiety, and their transmission across the generations. When we studied the children of the probands with major depression we found the children to be at high risk for numerous disorders, compared with the children of normal probands.[2]

Studies to determine risk in the offspring of depressed persons have suggested a close relationship between the adult and childhood forms of depression.[3-5] Similarly, an association between the adult and childhood forms of anxiety disorders has been suggested in reports from adult patients with anxiety disorders about their own childhood anxiety,[6-12] studies of the children of parents with anxiety disorders,[13] and studies of the adult parents of children with anxiety disorders.[10] Because of the inconsistency of the results of family studies, the relationship between depression and anxiety disorders, whether in adults or children, remains controversial.[1,14-16]

The results we report herein on the children of these probands parallel the findings we observed in the adult first-degree relatives of the probands. Depression plus panic or agoraphobia in adult probands conferred an increased risk of major depression and anxiety disorders in their young children. Taken together, these findings suggest an association between depression and anxiety disorders in some families across the entire age of risk for these disorders, including childhood.

SUBJECTS AND METHODS

Design

The subjects studied were the children, aged 6 to 17 years, of probands from a case-control, family-genetic study of affective

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disorders in adults. The probands of the children studied were adults (18 years and older) and derived from one of the following groups: major depressives (n=133) or a normal, never psychiatrically ill control group (n=82) drawn from a community sample in New Haven, Conn.

The proband groups were group matched by age and sex. All of the depressed probands were primary nonbipolar major depressives. The diagnostic assessment of the probands was based on Research Diagnostic Criteria following a modified Schedule for Affective Disorders and Schizophrenia—Lifetime version (SADS-L) interview. The full details of that study, including the design, diagnostic procedures, and findings, have been described elsewhere.[17-19]

Restratification of Probands by Anxiety Disorders

To determine the presence of a differential risk in relatives due to an accompanying anxiety disorder in the proband, the depressed probands were grouped according to the presence or absence of specific anxiety disorders, described in detail elsewhere.[1] Briefly, the depressed probands who did not have a concomitant anxiety disorder were initially placed in a "depression without an anxiety disorder" category. Because a substantial portion of the remaining depressed probands had received the diagnosis of having more than one anxiety disorder, a hierarchical scheme of agoraphobia over panic disorder over generalized anxiety disorder (GAD) was employed. Operationally, this meant that depressed probands with both agoraphobia and panic disorder would be classified as depressed with agoraphobia. Similarly, probands with both panic disorder and GAD would be classified as depressed with panic disorder.

There were not sufficient numbers of probands to create separate categories for depression plus simple or social phobia (n=6) or obsessive-compulsive disorder (n=4). These probands were classified using the hierarchical scheme according to whatever additional anxiety disorder diagnoses they had received. Operationally, this meant that four probands who originally had been classified as depressed with an anxiety disorder were reclassified as depressed without an anxiety disorder because they had the simple anxiety diagnoses that had been excluded from the hierarchy.

This reclassification of all probands yielded the following proband groups: normal, 82 subjects; depressed without anxiety disorder, 56; depressed plus agoraphobia, ten; depressed plus panic disorder, 22; and depressed plus GAD, 45. The number of probands from each group who had children aged 6 to 17 years (the focus of these analyses) were normal, 40; depressed without anxiety disorder, 23; depressed plus agoraphobia, ten; depressed plus panic, 11; and depressed plus GAD, 16.

Assessment of Children

In the family study of adults, comprehensive diagnostic estimates of probands, spouses, and all adult first-degree relatives, including children older than 18 years, were obtained blindly as to the status of the probands through direct interview, family history from multiple informants, and medical records when available.

Children younger than 18 years were not interviewed directly. Instead, information on minor children was obtained by family history from the proband, spouse, and other first-degree relatives.[2] The data presented on the children in this report always refer to the probands' children aged 6 to 17 years.

A screening instrument modified from the early work of Herjanic and Reich[20] was administered to the probands and spouses to determine symptoms of psychopathologic condition, behavioral problems, and psychological treatment in any of their children who were aged 6 to 17 years at the time of the proband interview. First, there was a general probe about problems with the child, and then a symptom list was read to the informant that covered questions about the child's psychological treatment, school difficulties, hyperactivity, delinquency, phobias, obsessions and compulsions, depression, suicidal behavior, bodily complaints, anxiety, psychotic symptoms, and substance abuse. Information was obtained separately for each child. Children under the age of 6 years were excluded from such assessment because of its inappropriateness for that age group. When there were positive answers to symptoms, the interviewers were instructed to code them and to record details in a narrative form as well. Medical records were also sought. For 64% of children with a diagnosis, information was available from more than one source. Agreement between parents on children's individual symptoms was excellent and ranged from 55% for complaints of bodily symptoms to 100% for child receiving medication. Agreement for depressive symptoms and for anxiety symptoms was also quite high (82% and 73%, respectively). For most other symptoms, there was agreement more than 80% of the time. There were no systematic differences between mothers and fathers in the reporting of children's symptoms.

Best-Estimate *DSM-III* Diagnosis of Children

A best-estimate diagnosis of the children based on *DSM-III* criteria was made by a psychiatrist (G.D.G.) with clinical training in child psychiatry. He was not involved in the original data collection and was blind to the clinical status of the proband. Included in the diagnostic process was a review of all the information that could be obtained about the child from medical records, from parents, and from other relative reports if they became available during an interview. The general method used to assign best-estimate diagnoses has been described elsewhere.[17]

RESULTS

Number of Probands, Age and Sex of Children

Table 1 gives the number of probands by presence or absence of anxiety disorder, by presence of children younger than 18 years, and by age and sex of the children. There were 215 probands. Of the 215, 100 probands had 194 children between the ages of 6 and 17 years. Although there was a greater number (63%) of older children (aged 13 to 18 years), reflecting the older age of the probands, there were nearly equal numbers of boys and girls. The mean number of children per proband (about two) was similar in the five proband groups, as were the age and sex distributions of the children by proband groups.

Characteristics of the Probands

Table 2 gives the sociodemographic and clinical characteristics of the probands. Of the probands, 57% were women; the mean age was 41 years; and 81% were currently married. The majority (69%) were Catholic. The mean age of onset of depression and of anxiety disorders was 26 and 30 years, respectively. The proband groups did not differ on sex, age, religion, or mean age of onset of depression or of anxiety disorders. The proband groups did differ on marital status and social class. That is, more of the probands with depression and no anxiety (39%) were separated and divorced, and more of the probands with depression plus GAD (50%) were from social classes I and II (Hollingshead Two-Factor Index of Social Class). However, these differences did not change the direction of the results, as will be shown in the analysis of the risk factors for disorders in the children.

Treatment and School Problems in Children

Table 3 gives the type of treatment and school problems in the children by proband group. The children of probands with depression plus panic disorder had received the most treatment for emotional problems (42.1%), followed by the children of probands with depression plus agoraphobia (33.3%), and depression only (26.3%). The children of probands with depression plus GAD and the children of normal subjects were similar in amount of treatment received (9.4% and 9.2%, respectively).

A range of treatments is represented. The same trends for treatment were not seen for school problems. School problems were highest in the children of probands with depression plus agoraphobia (27.8%) and depression only (23.7%). The children of probands with depression only had the highest percentage of school failures (15.8%). The children of probands with depression plus panic disorder had similar rates of school problems as did the children of normal subjects, 5.3% and 6.9%, respectively.

DSM-III Diagnoses in Children

Table 4 shows that the children of depressed probands had significantly more *DSM-III* diagnoses (range, 15.6% to 42.1%) than

Table 1.—Age and Sex of Children by Proband Group

Proband Group	No. of Probands	No. of Probands With Children (Aged 6-17 yr)	No. of Children at Risk	Children: Ages, % 6-12 yr	Children: Ages, % 13-18 yr	Children: Sex, % M	Children: Sex, % F
Normal	82	40	87	40	60	49	51
Depression, no anxiety disorder	56	23	38	29	71	53	47
Depression and agoraphobia	10	10	18	39	61	50	50
Depression and panic	22	11	19	37	63	47	53
Depression and generalized anxiety disorder	45	16	32	34	66	47	53
Total	**215**	**100**	**194**	37	63	49	51

Table 2.—Characteristics of Probands With Children Aged 6 to 17 Years

	Proband Group, % Normal (n=40)	Depression, No Anxiety Disorder (n=23)	Depression and Agoraphobia (n=10)	Depression and Panic Disorder (n=11)	Depression and GAD* (n=16)	Significance
Sex						
M	43	52	30	36	44	NS
F	57	48	70	64	56	
Age, yr, mean	42	43	44	45	41	NS
Marital status						
Married	90	61	90	73	87	$P<.05$
Separated, divorced	8	39	10	18	13	
Widowed	2	0	0	9	0	
Socioeconomic status†						
I, II	18	9	10	9	50	$P<.05$
III, IV, V	82	91	90	91	50	
Religion						
Catholic	77	70	67	64	56	
Protestant	20	13	11	9	31	NS
Jewish	3	4	0	18	0	
None or other	0	13	22	9	13	
Age at onset, major depression, yr, mean	. . .	30	26	20	26	NS
Age at onset, first anxiety disorder, yr, mean	. . .	. . .	29	31	32	NS

*Generalized anxiety disorder.
†Based on Hollingshead Two-Factor Index of Social Class.

the children of normal subjects (8.1%). The children of probands with depression plus panic disorder were the most affected (42.1%) as compared with the children of probands with depression plus agoraphobia (27.8%), depression and no anxiety disorder (21.1%), and depression plus GAD (15.6%). Although the rates of all disorders were generally higher among the children of probands with an anxiety disorder, significance levels were only computed for any diagnosis because of the small number of children in the individual diagnostic categories.

When specific disorders were examined separately, separation anxiety in the children of probands with depression plus panic disorder was the most frequent diagnosis (36.8%), followed by major depression (26.3%) in the same group. Major depression was also frequently found in the children of probands: 22.2% in the children of probands with depression plus agoraphobia; 10.5% in the children of probands with depression and no anxiety; 3.1% in the children of probands with depression and GAD. None of the children of the normal probands was noted to have major depression or separation anxiety. The children of probands with depression plus panic disorder and depression plus agoraphobia were also reported to have panic disorder, agoraphobia, or social phobia. These disorders were absent in the children of the other probands with the exception of one case of social phobia reported in a child of a normal proband.

The children of probands with depression plus agoraphobia or depression plus panic disorder, as compared with the other proband groups, also were found to have a relatively high number of "other disorders," 16.7% and 10.5%, respectively, as well as multiple (two or more) diagnoses, 27.8% and 31.6%, respectively.

Anxiety Disorders in the Children

Several of the children had both depression and anxiety disorders. Table 5 examines the rates of depression and anxiety disorders singly or together in children by proband diagnosis. The results show that the children's diagnoses tended to follow those of the probands: (1) There was increased depression in the children of the depressed probands, particularly the children of probands with depression plus agoraphobia and the children of probands with depression plus panic disorder (22.2% and 26.3%, respectively). (2) There was increased anxiety disorder in the children of the probands with depression plus panic disorder. (3) The children of probands with depression and no anxiety disorder did not themselves have anxiety disorders. (4) Increased rates of phobia were observed in the children of probands with depression plus

Table 3.—Type of Treatment and School Problems in Children by Proband Group

	Proband Group, Rate per 100 in Children					
	Normal (n=87)	Depression, No Anxiety Disorder (n=38)	Depression and Agoraphobia (n=18)	Depression and Panic Disorder (n=19)	Depression and GAD* (n=32)	Significance
Any treatment received by children for an emotional problem						
Child guidance clinic	0	7.9	11.1	10.5	3.1	$P<.05$
School counselor	3.5	7.9	0	10.5	0	NS
Psychiatrist	0	5.3	11.1	5.3	0	$P<.05$
Family agency	0	5.3	16.7	0	0	$P<.001$
Pediatrician	4.6	5.3	11.1	6.3	16.7	NS
Other	1.2	7.9	11.1	15.8	0	$P<.05$
Any of above	9.2	26.3	33.3	42.1	9.4	$P<.05$
School problems of children						
Failed or repeated grade	4.6	15.8	5.6	0	3.1	$P<.10$
Slow learner	1.2	7.9	5.6	0	0	NS
Truant	1.2	7.9	11.1	5.3	0	$P<.10$
Suspended or expelled	1.2	2.6	0	0	0	NS
Any of above	6.9	23.7	27.8	5.3	12.5	NS

*Generalized anxiety disorder.

Table 4.—Rates of *DSM-III* Diagnoses Among Children

	Proband Group, Rate per 100 in Children				
Best-Estimate *DSM-III* Diagnosis in Child	Normal	Depression, No Anxiety	Depression and Agoraphobia	Depression and Panic	Depression and GAD*
Major depression	0	10.5	22.2	26.3	3.1
Separation anxiety	0	0	11.1	36.8	6.3
Panic disorder	0	0	5.6	5.3	0
Agoraphobia	0	0	5.6	5.3	0
Social phobia	1.2	0	11.1	5.3	0
Simple phobia	0	0	0	5.3	0
Obsessive-compulsive	1.2	0	5.6	0	0
Attention deficit disorder	1.2	13.2	11.1	5.3	9.4
Conduct disorder	1.2	10.5	11.1	0	3.1
Substance abuse	0	5.3	11.1	0	0
Developmental reading	3.5	2.6	11.1	0	6.3
Other diagnosis	0	2.6	16.7	10.5	0
Any diagnosis	8.1	21.1	27.8	42.1	15.6†
One diagnosis	8.1	7.9	0	10.5	6.3
Two or more diagnoses	0	3.1	27.8	31.6	9.3

*Generalized anxiety disorder.
†$P<.01$.

agoraphobia and among the children of probands with depression plus panic disorder. (5) There were increased co-occurrences of depression plus any anxiety disorder in the children of probands who also had the co-occurrence of depression and an anxiety disorder, particularly panic disorder.

Depression and Anxiety by Sex of Child and Proband

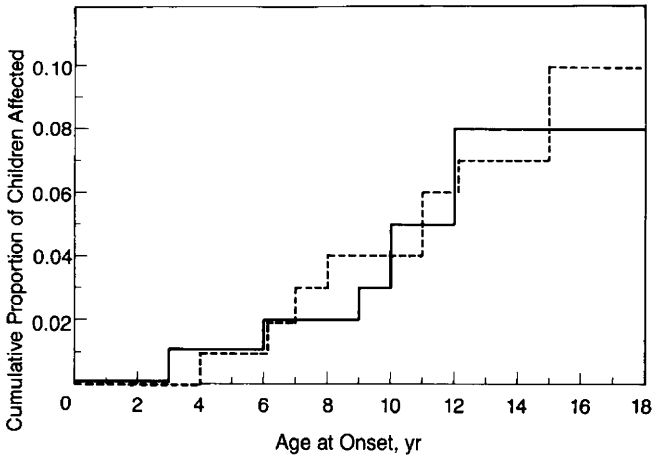
Age-corrected rates of depression and any anxiety disorder by sex were calculated for the children of probands using Lifetime Risk (LTR), which is defined as the risk of onset of a particular disorder between birth and some particular age (age 18 years in this case). The estimation of LTR is based on the nonparametric product-limit table method for analyzing survivorship of Kaplan and Meier,[21] which yields a maximum likelihood estimate of LTR. This method makes a calculation at each point in time when there is a change in the number of persons at risk for development of the disorder. The number at risk changes with each onset of the disorder and with each death of an unaffected person.[22] The Biomedical Computer Program P-series (BMDP) program PIL was used to calculate LTR.[23]

The Figure depicts the cumulative proportion of male and female children affected with any anxiety disorder. The earliest onset age of an anxiety disorder was 3 years. The LTR by age 18 years for developing an anxiety disorder was .08 among boys and .10 among girls. There were no differences in rates of anxiety disorders by sex of child. Similar analyses presented elsewhere[2] for the LTR average age for the development of major depression found no significant sex differences in patterns of age of onset. The LTR by age 18 years for development of major depression was .12 among the boys of probands, and .13 among the girls of probands, slightly higher than for anxiety disorders. The earliest age of onset of depression was 6 years, slightly older than for anxiety.

Table 5.—Rates of *DSM-III* Anxiety Disorders and Depression Among Children

Best-Estimate *DSM-III* Diagnosis in Child	No. Children With Diagnosis	Proband Group, Rate per 100 in Children				
		Normal	Depression, No Anxiety Disorder	Depression and Agoraphobia	Depression and Panic	Depression and GAD*
Any major depression	17	0	13.2	22.2	26.3	9.4
Any anxiety disorder†	13	2.3	0	11.1	36.8	6.3
Any phobia‡	5	1.2	0	11.1	10.5	0
Major depression and any anxiety disorder	8	0	0	11.1	26.3	3.1

*Generalized anxiety disorder.
†All phobias, panic, separation anxiety, and obsessive-compulsive included.
‡Agoraphobia, simple, and social phobia included.



Risk of any anxiety disorder in children by age 18 years. Solid line indicates boys; broken line, girls.

Using logistic analyses, we also examined the effect of sex of proband on the rates of any anxiety disorder or any depression in children, and found no significant effect. Caution must be exhibited in interpreting these findings because of the small sample size of children who were affected and the retrospective nature of the data.

Proband Characteristics as Risk Factors for Illness in Children

Several proband characteristics (eg, sociodemographic variables, early history, and family history of illness) were examined to determine whether these proband characteristics increased the risk of major depression, any anxiety disorder, or any *DSM-III* diagnosis in the children across the proband groups (Table 6). The proband characteristics that did not increase the risk were current age, sex, social class, number of children (any age) in family, marital status, childhood history of stuttering or sleepwalking, and separation from parent as a child.

The characteristics of probands that did increase risk in children were number of episodes of depression, childhood history of enuresis, and number of first-degree relatives (ie, probands' parents, siblings, or adult children, or children's grandparents, aunts, uncles, and adult siblings) with major depression or anxiety disorders.

Having found that the proband's number of episodes of depression significantly increased major depression in the child, we conducted the following analysis to determine if the child's age at exposure or years of exposure to parental illness were critical in increasing risk. We first examined the relationship between the child's age at exposure to the parent's first onset of depression and of anxiety. We next examined the number of years the child had been exposed to the proband's depression and anxiety. Neither set of analyses yielded any significant differences in rates of disorders in the children, nor were there any interpretable trends.

COMMENT

In our family case-control study of the adult first-degree relatives of probands with major depression, we adopted the following strategy for understanding the relationship between depression and anxiety disorders.[1,4] We studied the adult first-degree relatives of the normal proband group, of the probands with major depression alone, and of the probands with major depression plus agoraphobia, panic disorder, or GAD, to see whether depression plus an anxiety disorder would predict differential rates and/or specific types of transmission of disorders in relatives. This strategy was fruitful because we found that depression and panic in the proband were associated with remarkably high rates of depression and anxiety disorders among the first-degree adult relatives. The results argued for a partially shared diathesis between panic and some cases of major depression.[1]

In this study we applied the same methods to assess the rates of psychiatric disorders among the proband's children, ages 6 to 17 years. While the children samples are fewer in number than were the adult first-degree relatives, the results are parallel. We found the following: (1) The children of depressed probands as compared with the children of normal probands were at increased risk for major depression. (2) Depression plus agoraphobia or panic disorder in the probands conferred an additional risk on the children. If the proband had both depression and panic disorder, the children were at the greatest risk for receiving psychiatric treatment and for having a psychiatric disorder, particularly major depression and separation anxiety. Over one third of the children of probands with depression plus panic disorder had separation anxiety, and over one fourth had major depression. (3) There was a specificity to the transmission of anxiety and depression in children. Any anxiety disorder was more frequent in the children of probands with depression and panic disorder. Any phobia was more frequent in the children of probands with depression and either agoraphobia or panic. Depression and anxiety disorder were more frequent in the children of probands who had both of these disorders, particularly depression and agoraphobia or panic disorder. Generalized anxiety disorder in probands differed in that it only slightly increased the risk of either depression or anxiety disorder in the children. (4) There were no sex differences in risk of depression or of anxiety disorder in the children, no specific sex patterns in age of onset, and no sex of proband effect on rates of depression and anxiety in the children. These findings require replication in a larger sample. (5) The proband

Table 6.—Proband Characteristics and *DSM-III* Diagnosis in Their Children

Proband Characteristics	*DSM-III* Diagnosis in Children*				Significance
	Major Depression	Any Anxiety	Any Other Diagnosis	No Diagnosis	
Mean age, yr	43	44	41	41	NS
Sex,					
M	6.3	2.5	5.0	86.3	NS
F	7.9	3.5	7.9	80.7	
Social class,† mean	3.2	3.0	3.3	3.5	NS
Mean No. offspring in family	3.4	4.0	3.8	3.5	NS
Marital status, %					
Currently married	6.2	2.5	5.6	85.8	NS
Currently unmarried	12.5	6.3	12.5	68.7	
Mean No. episodes of depression	3.6	2.2	2.5	2.0	$P<.001$
Childhood history of enuresis, %					
Yes	23.5	5.9	11.8	58.8	$P<.01$
No	5.0	2.8	6.2	85.3	
Childhood history of stuttering, %					
Yes	0.0	10.0	0.0	90.0	NS
No	7.6	2.7	7.1	82.6	
Childhood history of sleepwalking, %					
Yes	6.7	3.3	6.7	83.3	NS
No	7.3	3.1	6.7	82.9	
Separated from parent during childhood, %					
Yes	9.7	1.6	3.2	85.5	NS
No	6.1	3.8	8.3	81.8	
Mean No. first-degree relatives psychiatrically ill	3.9	3.3	2.8	2.1	$P<.05$
Mean No. first-degree relatives depressed	1.7	0.8	0.9	0.6	$P<.05$
Mean No. first-degree relatives with anxiety disorders	1.5	1.0	1.0	0.5	$P<.001$

*Mutually exclusive diagnosis.
†Based on Hollingshead Two-Factor Index of Social Class.

characteristics that did not increase risk of depression, anxiety disorder, or any psychiatric disorder in children were current age, sex, social class, or marital status; number of other children; childhood history of stuttering or sleepwalking; or separation from parents during childhood. The child's age at exposure or years of exposure to parental illness also did not increase risk. (6) The proband characteristics that signficiantly increased risk to children were recurrent depressions, high familial loading of major depression or any anxiety disorder, and childhood history of enuresis.

Limitations

The substantive findings of this study should be viewed against its methodologic limitations. Direct interviews with children, and teachers' reports, are lacking. Because these rates are based on family history, they are probably underestimates.[18,24] Detailed assessment of children's social functioning, personality, and social supports that may contribute to outcome are lacking. Parents with psychiatric disorders may be less tolerant of symptomatic behavior on the part of the children and, hence, may report more symptoms in their children than would normal control parents. On the other hand, agreement between parents on their child's symptoms was reasonably good, and the best estimates of *DSM-III* diagnoses were based on information from multiple sources, not just from the ill parent.

Though the interviewers collecting symptom data were not blind to the status of the proband, they were blind to the status of the spouse and other informants who were also providing information on the children. Most important, the best-estimate diagnoses based on information from multiple sources were made by a psychiatrist who was blind to the clinical status of both parents and all first-degree relatives and who was not involved in the original design or data collection of the study. However, we are now collecting more comprehensive data through direct interviewing of these children, through interviews of both parents about the children, and from health providers and schools. Several questions are raised by these data.

Are Adult and Childhood Anxiety Disorders Similar?

Our data suggest that the children of patients with agoraphobia or panic disorder are beginning to manifest similar disorders themselves, particularly separation anxiety. A number of investigators have made similar observations about the onset of adult anxiety disorder in childhood or early adulthood. One of the earliest observations was by Klein in his 1964 review of 32 adult patients being treated for panic attacks, with agoraphobia or anticipatory anxiety.[11] At least half of the adult patients reported marked separation anxiety and difficulty in adjusting to school as children. The patients who reported childhood separation anxiety had chronically high levels of separation anxiety throughout their lives and suffered significantly more panic attacks under conditions of separation and bereavement.

Roth,[25] in a study of 135 patients with phobic anxiety and depersonalization, noted that the commonest age of onset was in the early 20s. Sheehan et al,[26] in a study of 100 patients treated for agoraphobia and panic attacks, found that 55% had an onset of agoraphobia by age 20 years. Buglass et al,[27] in a study of 30 agoraphobic housewives,

dated the mean age of onset of agoraphobic symptoms at 31 years, with a range of 10 to 52 years. Agras et al,[28] in a community survey of 325 persons, found a high prevalence of fears and phobia in children younger than 14 years and a differential pattern by age. A fear of doctors, injection, darkness, and strangers was short-lived and had a sharply declining incidence with age. A fear of animals, heights, storms, enclosed places, and social situations showed slowly declining incidence with age, suggesting that, once acquired, such fears were long-lived.

Others have questioned whether childhood anxiety symptoms were related to adult anxiety disorders or to nonspecific psychiatric problems. Berg et al[7] surveyed 786 female members of an agoraphobia correspondence club to learn about incidence of past school phobias. When these women were compared with 58 nonagoraphobic women who were psychiatric outpatients with a neurotic disorder, few differences between the groups were found. A history of school phobias was equally common in both groups. The authors concluded that childhood school phobias were related to adult neurotic illness rather than specificity to adult agoraphobia.

Tyrer and Tyrer[12] interviewed 60 phobic, 60 anxious, and 120 depressed adult patients, against 120 matched orthopedic and dental patients, about problems of childhood school attendance due to refusal. They found that school refusal occurred more frequently among the patients with psychiatric disorders. There was a nonsignificant tendency for childhood school refusal to be higher in phobic patients. These authors concluded, in agreement with Berg,[13] that there is a link between childhood school refusal and adult neurotic illness. However, the diagnostic criteria for neurotic illness in these studies were unclear. Many of these nonagoraphobic neurotic women might have been suffering from other anxiety or depressive disorders.

Klein's[11] early observations of the possible relationship between adult and childhood anxiety disorders, and the successful treatment of these adult anxiety patients with imipramine, led to the first trial of imipramine in school-phobic children by Gittleman-Klein and Klein.[10] Their results suggested that school-phobic children and phobic anxious adults may share a common psychopathologic process as both adults and children with phobic problems had a similar positive response to imipramine. However, we agree with the investigators' conclusion about the need for long-term studies of phobic children to determine to what degree these disorders were precursors to adult anxiety or to depressive states.[9,10]

Do Adult Anxiety Disorders Transmit to Children?

Our study suggested that some adult anxiety disorders transmitted anxiety and depression to children. To our knowledge, there has been no systematic, blind, case-control study of the young children of adult probands with anxiety disorder or of the adult parents of children with anxiety disorder. Relevant data are available from a few small studies.

Berg et al[8] studied the incidence of past school phobias in the children (aged 7 to 15 years) of agoraphobic women and found an increased risk of children with school phobias (about 14%). The risk in children was increased further if the mother herself also had school phobias as a child.

Berg et al[7] reported on the maternal psychiatric illness of 113 adolescent inpatients with school phobias, compared with 113 adolescent inpatients with nonschool phobic problems. About a fifth of parents in both groups had a history of psychiatric illnesses, more than half of which were affective disorders. The authors concluded that there was no specific association between type of parental psychiatric illness and type of childhood disorder. However, the use of case records and letters from physicians as the data source would limit the strength of the findings.

Gittelman-Klein[9] studied parents of school-phobic and of hyperactive children. Parents were probed about depressive episodes, phobic symptoms, particularly school phobias, or separation anxiety with regard to themselves and to the patients' siblings. There was a significant increase of separation anxiety in the parents and of school phobias in the siblings of the phobic children.

There have been several studies of the children of psychiatrically ill patients[29] and the children of depressive patients.[2,3,5,30-37] In general, these studies found that children of parents with a major affective disorder were at significant risk for depression. As most of the studies focused on depression in both the parents and the children, with few exceptions data on anxiety disorders in the children were often not reported. Moreover, none of the studies included an assessment of any accompanying anxiety disorders in the depressed probands. If the convention of not diagnosing anxiety disorder if it occurs with depression were followed, then the anxiety disorders would have been missed in the depressed parent probands, further obscuring findings of anxiety in the children.

Conners et al[30] noted an increase of anxiety symptoms (disorders were not studied) in the offspring of female nonbipolar depressive patients and an overall increase in anxiety symptoms of female offspring. Cytryn et al[34] found that in three of 13 index families children had overanxious or phobic disorders. This contrasted with one case of overanxious disorder in 13 control families. McKnew et al[32] reported that 10% of the children of bipolar and unipolar depressive patients had anxiety symptoms. O'Connell et al,[37] in a nonblind trial of 22 children (aged 6 to 17 years) of bipolar probands, found that separation anxiety was a characteristic of the entire group of children, including clinging behavior, fear of dark, unwillingness to sleep alone, and difficulty separating from parents.

Are All Anxiety Disorders Alike?

We found support for a distinction between GAD and panic or agoraphobia. In the proband, GAD, when compared with panic or agoraphobia, conferred a much lower risk of an anxiety disorder in the children. Our findings are consistent with a recent report by Raskin et al[38] that patients with panic disorder and GAD differed in their early childhood environment as well as in the incidence of depressive episodes.

Are Anxiety and Depression Related?

This study in children, similar to our parallel study of adults,[1] suggests a relationship between depression and anxiety disorders. Whereas anxiety disorder in an adult conferred an increased risk of major depression in the children, major depression without an anxiety disorder in the parent did not increase risk of anxiety disorder in the children. Recent data by Crowe et al[16] suggest that the adult relatives of probands with panic disorder have increased rates of secondary, but not primary, depression. Without a similar study of children of probands with panic and with agoraphobia alone, we can only speculate about the full relationship between depression and anxiety in adults and children.

CONCLUSION

We have found that depression in the parent increased the risk of depression in the children aged 6 to 17 years, and that depression plus anxiety disorders, particularly panic and agoraphobia, conferred an additional risk of depression and anxiety in these children. Depression and GAD in the proband only minimally increased the risk in children, suggesting either a distinction between GAD and the other anxiety disorders or the unreliability of the diagnosis of GAD. This finding on the minimal increase of risk in children aged 6 to 17 years of probands with depression and GAD was not found in adult relatives of these probands, and requires further examination.[1] Panic disorder in the parents, in contrast to other anxiety disorders, conferred a greater than threefold increase of separation anxiety in the children. Familial loading and recurrent depression in the parent also increased the risk to children.

Our findings need to be taken into account in future studies of children of depressed and/or anxious parents. Our findings also suggest the use of a longitudinal, direct-interview study of children of probands with depression and anxiety disorders, and with anxiety disorders alone, to sort out the relationship between depression and anxiety as well as the relationship between the adult and childhood anxiety disorders. Moreover, future family studies of depressed probands should carefully document any accompanying anxiety disorders in both the proband and the relatives.

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References

1. Leckman JF, Weissman MM, Merikangas KR, Pauls DL, Prusoff BA: Panic disorder and major depression: Increased risk of depression, alcoholism, panic and phobic disorders in families of depressed probands with panic disorder. *Arch Gen Psychiatry* 1983;40:1055-1060.
2. Weissman MM, Prusoff BA, Gammon GD, Merikangas KR, Leckman JF, Kidd KK: Psychopathology in the children (ages 6-18) of depressed and normal parents. *J Am Acad Child Psychiatry* 1984;23:78-84.
3. Orvaschel H: Parental depression and child psychopathology, in Guze SB, Earls FJ, Barret JE (eds): *Childhood Psychopathology and Development*. New York, Raven Press, 1983, pp 53-66.
4. Weissman MM, Paykel ES, Klerman GL: The depressed woman as a mother. *Soc Psychiatry* 1972;7:98-108.
5. Beardslee WR, Bemporad J, Keller MB, Klerman GL: Children of parents with major affective disorder: A review. *Am J Psychiatry* 1983; 140:825-832.
6. Gittelman-Klein R, Klein DF: School phobia: Diagnostic considerations in the light of imipramine effects. *J Nerv Ment Dis* 1973;156:199-215.
7. Berg I, Butler A, Pritchard J: Psychiatric illness in the mothers of school-phobic adolescents. *Br J Psychiatry* 1974;125:466-467.
8. Berg I, Marks I, McGuire R, Lipsedge M: School phobia and agoraphobia. *Psychol Med* 1974;4:428-434.
9. Gittelman-Klein R: Psychiatric characteristics of the relatives of school phobic children, in Siva Sankar DV (ed): *Mental Health in Children*. New York, PJD Publications Inc, 1975, vol 1, pp 325-334.
10. Gittelman-Klein R, Klein DF: Separation anxiety in school refusal and its treatment with drugs, in Hersov L, Berg I (eds): *Out of School*. New York, John Wiley & Sons Inc, 1980, pp 321-341.
11. Klein DF: Delineation of two-drug-responsive anxiety syndromes. *Psychopharmacologia* 1964;5:397-408.
12. Tyrer P, Tyrer S: School refusal, truancy, and adult neurotic illness. *Psychol Med* 1974;4:416-421.
13. Berg I: School phobia in the children of agoraphobic women. *Br J Psychiatry* 1976;128:86-89.
14. Leckman JF, Merikangas KR, Pauls DL, Prusoff BA, Weissman MM: Anxiety disorders and depression: Contradictions between family study data and *DSM-III* conventions *Am J Psychiatry* 1983;140:880-882.
15. Munjack DJ, Moss HB: Affective disorder and alcoholism in families of agoraphobics. *Arch Gen Psychiatry* 1981;38:869-874.
16. Crowe RR, Noyes R, Pauls DL, Slymen D: A family study of panic disorder. *Arch Gen Psychiatry* 1983;40:1065-1069.
17. Leckman JF, Sholomskas D, Thompson WD, Belanger A, Weissman MM: Best estimate of lifetime psychiatric diagnosis: A methodological study. *Arch Gen Psychiatry* 1982;39:879-883.
18. Weissman MM, Kidd KK, Prusoff BA: Variability in rates of affective disorders in relatives of depressed and normal probands. *Arch Gen Psychiatry* 1982;39:1397-1403.
19. Weissman MM, Gershon ES, Kidd KK, Prusoff BA, Leckman JF, Dibble E, Hamovitt J, Thompson WD, Pauls DL, Guroff JJ: Psychiatric disorders in the relatives of probands with affective disorders: The Yale-National Institute of Mental Health Collaborative Study. *Arch Gen Psychiatry* 1984;41:13-21.
20. Herjanic B, Reich W: Development of a structured psychiatric interview: Agreement between child and parent on individual symptoms. *J Abnorm Child Psychol* 1982;10:307-324.
21. Kaplan EL, Meier P: Nonparametric estimation from incomplete observations. *J Am Stat Assoc* 1958;53:457.
22. Thompson WD, Weissman MM: Quantifying lifetime risk of psychiatric disorder. *J Psychiatr Res* 1981;16:113-126.
23. Dixon WJ (ed): *BMDP Statistical Software*. Berkeley, Calif, University of California Press, 1981.
24. Thompson WD, Orvaschel H, Prusoff BA, Kidd KK: An evaluation of the family history method for ascertaining psychiatric disorders. *Arch Gen Psychiatry* 1982;39:53-58.
25. Roth M: The phobic anxiety-depersonalization syndrome and some general aetiological problems in psychiatry. *J Neuropsychiatry* 1960;12: 293-306.
26. Sheehan DV, Sheehan KE, Minichiello WE: Age of onset of phobic disorders: A reevaluation. *Compr Psychiatry* 1981;22:544-553.
27. Buglass D, Clarke J, Henderson AS, Kreitman N, Presley AS: A study of agoraphobic housewives. *Psychol Med* 1977;7:73-86.
28. Agras S, Sylvester D, Oliveau D: The epidemiology of common fears and phobia. *Compr Psychiatry* 1969;10:151-156.
29. Rutter M: *Children of Sick Parents: An Environmental and Psychiatric Study*. Maudsley Monographs 16, Institute of Psychiatry. London, Oxford University Press, 1966.
30. Conners CK, Himmelhock J, Goyette CH, Ulrich R, Neil JF: Children of parents with affective illness. *J Am Acad Child Psychiatry* 1979;18: 600-607.
31. Greenhill LL, Shopsin B, Temple H: Children of affectively ill parents: Psychiatric status determined by structured interview. *Psychopharmacol Bull* 1980;16:23-24.
32. McKnew DH, Cytryn L, Efron AM, Gershon ES, Bunney WE Jr: Offspring of patients with affective disorders. *Br J Psychiatry* 1979;134: 148-152.
33. Welner Z, Welner A, McCrary MD, Leonard MA: Psychopathology in children of inpatients with depression: A controlled study. *J Nerv Ment Dis* 1977;164:408-413.
34. Cytryn L, McKnew DH, Bartko JJ, Lamour M, Hamovitt J: Offspring of patients with affective disorders: II. *J Am Acad Child Psychiatry* 1982;21:389-391.
35. Kestenbaum CJ: Children and adolescents at risk for manic-depressive illness: Introduction and overview. *Adolesc Psychiatry* 1982;10:245-255.
36. Kron L, Decina P, Kestenbaum CJ, Farber S, Gargan M, Fieve R: The offspring of bipolar manic-depressives: Clinical features. *Adolesc Psychiatry* 1982;10:273-291.
37. O'Connell RA, Mayo JA, O'Brien JD, Misrsheidaie F: Children of bipolar manic-depressives, in Mendlewicz J, Shopsin B (eds): *Genetic Aspects of Affective Illness*. New York, SP Medical & Scientific Books, 1979, pp 55-68.
38. Raskin M, Peeke HVS, Dickman W, Pinsker H: Panic and generalized anxiety disorder: Developmental antecedents and precipitants. *Arch Gen Psychiatry* 1982;39:687-689.