

Patterns of Psychopathology and Dysfunction in High-Risk Children of Parents With Panic Disorder and Major Depression

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Objective: The purpose of the study was to evaluate 1) whether an underlying familial predisposition is shared by all anxiety disorders or whether specific risks are associated with specific disorders, and 2) whether panic disorder and major depression have a familial link.

Method: The study compared four groups of children: 1) offspring of parents with panic disorder and comorbid major depression (N=179), 2) offspring of parents with panic disorder without comorbid major depression (N=29), 3) offspring of parents with major depression without comorbid panic disorder (N=59), and 4) offspring of parents with neither panic disorder nor major depression (N=113).

Results: Parental panic disorder, regardless of comorbidity with major depression, was associated with an increased

risk for panic disorder and agoraphobia in offspring. Parental major depression, regardless of comorbidity with panic disorder, was associated with increased risks for social phobia, major depression, disruptive behavior disorders, and poorer social functioning in offspring. Both parental panic disorder and parental major depression, individually or comorbidly, were associated with increased risk for separation anxiety disorder and multiple (two or more) anxiety disorders in offspring.

Conclusions: These findings confirm and extend previous results documenting significant associations between the presence of panic disorder and major depression in parents and patterns of psychopathology and dysfunction in their offspring.

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Although several studies have shown that the young offspring of parents with anxiety disorders are at increased risk for anxiety disorders (1-6), uncertainties remain as to the nature of this risk. One question regards its specificity: is there an underlying familial predisposition shared by all anxiety disorders or are there specific risks for specific anxiety disorders?

The idea that a general "anxiety proneness" may be transmitted has been hypothesized by several authors (7-9). Support for this hypothesis derives from family (2, 10) and twin (7, 11) studies suggesting that familial or genetic diatheses confer risk for anxiety disorders in general but not for specific disorders. The high rates of comorbidity within the anxiety disorders observed among adults (12-14) and children (15), as well as findings documenting similar patterns of comorbidity between anxiety disorders of childhood and adulthood (16-19), lend further support. However, some data have suggested specificity of transmission for anxiety disorders. Evidence from family studies has suggested specific aggregation for panic disorder (10, 20, 21), generalized anxiety disorder (22, 23), social phobia (24, 25), and other phobic disorders (26). Still other studies either have supported contributions of both general and specific diatheses (27) or have suggested different patterns of association for different anxiety disorders (28,

29). Clearly, further work is needed to resolve this important issue.

A second and related question pertains to diagnostic homogeneity of parental groups. Some researchers combined data for offspring of parents with heterogeneous anxiety disorders (2, 4). However, if different parental anxiety disorders have different underlying diatheses, they may be associated with different patterns of risk to offspring. Therefore, the next phase of work ought to focus on diagnostically homogeneous parental groups, while examining a variety of anxiety disorders in the offspring as outcomes.

A third major question concerns the association between anxiety disorders and major depression, disorders that have been observed to be highly comorbid (30). The ambiguous relationship between these conditions is reflected in the literature on children at risk by the limited and somewhat contradictory data about the contribution of parental major depression to the risk for anxiety disorders in the offspring. For example, although Turner et al. (2) found that children of parents with agoraphobia or obsessive-compulsive disorder were more likely than children of parents with dysthymia to have childhood anxiety disorders, Sylvester et al. (5) and Beidel and Turner (4) reported similar rates of anxiety disorders in children of pa-

tients with anxiety disorders and major depression. Breslau et al. (31), in an epidemiological study, found that children of mothers with major depression, but not with generalized anxiety disorder, had increased rates of over-anxious disorder and major depression.

On the other hand, our group reported that parental panic disorder with agoraphobia increased the risk for both anxiety disorders and major depression in the offspring, whereas parental major depression increased the risk selectively for major depression but not for anxiety disorders (3). Similar results were reported by Weissman et al. (1), who found an increased risk for anxiety disorders in children whose parents had a diagnosis of major depression and comorbid agoraphobia or panic disorder, while children of parents with major depression only or of normal comparison parents had very low rates of anxiety disorders. These contradictory findings call for more research.

Delineating the spectrum of psychopathology and dysfunction in children at risk for anxiety disorders has clinical, scientific, and public health implications. Clarifying the type and severity of anxiety and related disorders in children of parents with specific anxiety disorders may lead to the development of preventive interventions for children at high risk for specific anxiety disorders. Focusing on young offspring could allow the development of early interventions that could be administered before these conditions become chronic and difficult to treat. Moreover, clarifying the putative familial link between anxiety and depressive disorders in parents and children at risk may lead to a better understanding of the comorbidity between these disorders.

The present study sought to address the limitations of prior studies with a study of young high-risk children, selected through parents with panic disorder or major depression. The study evaluated multiple domains of functioning in these children and in comparison subjects whose parents had neither panic disorder nor major depression. On the basis of prior literature, we hypothesized that parental panic disorder would confer a risk for both panic disorder and major depression and that parental major depression would confer a risk for major depression but not panic disorder.

Method

Subjects

We recruited three groups of parents who had at least one child age 2–6 years: 1) 131 parents treated for panic disorder and their 227 children, 2) 61 comparison parents with neither major anxiety nor mood disorders and their 119 children, and 3) 39 parents treated for major depression who had no history of either panic disorder or agoraphobia and their 67 children. The children ranged in age from 2–25 years. Of the 131 panic disorder families, 113 had either one parent with comorbid panic disorder and major depression (N=102) or one parent with panic disorder and another with major depression (N=11). Assessments of psychopathology and/or dysfunction were available for 380 of the 413

children (92.0%). Therefore, comparisons were made between four groups: 1) children of parents with both panic disorder and major depression (N=179), 2) children of parents with panic disorder without comorbid major depression (N=29), 3) children of parents with major depression without comorbid panic disorder (N=59), and 4) children of parents with neither panic disorder nor major depression (N=113).

We recruited parents with panic disorder and major depression from clinical referrals and advertising by using a three-stage ascertainment procedure. The first stage was implicit in the patient's referral to a clinic or response to an advertisement calling for adults in treatment for panic disorder or major depression. The second step consisted of screening the patient by telephone to document the presence of the full DSM-III-R criteria for panic disorder or major depression. Patients who met the criteria for these disorders were recruited for a complete structured psychiatric interview. Only patients who received a positive lifetime diagnosis of panic disorder or major depression by psychiatric interview and who had been treated for these disorders were included.

We recruited comparison parents who were free of major anxiety disorders (panic disorder, agoraphobia, social phobia, or obsessive-compulsive disorder) or mood disorders (major depression, bipolar disorder, or dysthymia) through advertisements to hospital personnel and in community newspapers. We screened these adults in three stages. The first stage was implicit in the fact that hospital personnel or respondents to advertisements should have rates of panic disorder or major depression no higher than the rates in the general population. The second stage was the telephone screen described earlier. The prospective comparison subjects were then administered a psychiatric interview. This study was approved by the institutional review board of the hospital where the study was based, and all participants (parents) signed written consent.

Procedures

We conducted psychiatric assessments of children age 5 and older (N=312) by completing the Schedule for Affective Disorders and Schizophrenia for School-Age Children—Epidemiologic Version (K-SADS-E) (32) with the mothers. Children age 12 and older (N=11) were interviewed directly by a separate interviewer. We combined data from direct and indirect interviews and considered a diagnostic criterion positive if it was endorsed in either interview. We conducted direct psychiatric assessments with each parent by using the Structured Clinical Interview for DSM-III-R (33). We documented the degree of impairment associated with each diagnosis and the type of treatment obtained. We assessed socioeconomic status with the Hollingshead Four-Factor Index (34), which includes information about both parents' educational levels and occupations.

Interviews were conducted by raters with a bachelor's degree in psychology under the supervision of the two senior investigators (J.F.R. and J.B.). The raters underwent a training program in which they were required to 1) master the diagnostic instruments, 2) learn about DSM-III-R criteria, 3) watch training tapes, 4) participate in interviews performed by experienced raters, and 5) rate several subjects under the supervision of the project coordinator. The raters received continued supervision of their assessments from senior project staff and audiotaped all interviews for later random checking. Kappa coefficients of agreement were computed between the interviewers and the board-certified psychiatrists who listened to the audiotaped interviews. For 173 interviews, the median kappa was 0.86. Diagnoses for all subjects were made on the basis of a consensus judgment by the two senior investigators (J.B. and J.F.R.).

Children were evaluated by interviewers blind to the diagnostic status of the parents. Blinded evaluation was assured as follows:

1) only the project coordinator knew the diagnostic category of the parent; 2) psychiatric interviewers of parents were blind to the ascertainment status of the parent (e.g., panic disorder patient, major depression patient, comparison subject, spouse), as well as to all information about the children; 3) interviewers who gathered data on children from the children's mothers or from the children themselves were blind to all diagnostic information about the parents, including their ascertainment status; and 4) the final diagnoses for all subjects (parents and children) were made by clinicians who were blind to the subjects' original recruitment group, to all nonpsychiatric data collected from the individual being diagnosed, and to all information about other family members.

In addition, we collected dimensional measures of psychopathology in children age 2 and older by having the mothers complete the Child Behavior Checklist in separate versions for preschoolers (2–3 years old) and for school-age children (4–18 years old) (35, 36). For the purpose of this analysis, we combined data from the corresponding scales in the two versions of the Child Behavior Checklist. One advantage of the Child Behavior Checklist as a measure of psychopathology is that, unlike diagnoses, which focus on clinically serious symptoms, the Child Behavior Checklist can also capture milder levels of symptoms. To capitalize on this feature of the Child Behavior Checklist, we used a T score of ≥ 60 (i.e., one standard deviation above the mean) to signify impairment.

We also assessed the following areas of functioning in children over age 5:

6. Social functioning was assessed with the Global Assessment of Functioning scale of DSM-III-R and the Social Adjustment Inventory for Children and Adolescents (37). The Social Adjustment Inventory for Children and Adolescents is a semi-structured interview that assesses adaptive functioning in children and adolescents and covers the four major role areas of school functioning, spare time activities, peer relations, and home life.
7. School functioning was measured by three indices: placement in a special class, use of in-school resource-room tutoring, and having to repeat grades.
8. Treatment history information was obtained by inquiring while administering the K-SADS-E questions about the nature and duration of treatment the child had received.

Statistical Analyses

We first compared children from the four parental diagnostic groups on potentially confounding demographic variables (age, gender, socioeconomic status, size of sibship, intactness of family, and race/ethnicity). Then we examined differences in psychopathology and functioning between children from the four parental ascertainment groups while controlling for potential demographic confounds. Multiple members of a single family (i.e., members of the same sibship) cannot be considered independent of one another because they share genetic, cultural, and social risk factors. To deal with this problem, for all comparisons we used the generalized estimating equation method to estimate general linear models (38), controlling for one or more potentially confounding variables where necessary, as implemented in Stata (39). We used Wald's chi-square test to assess the statistical significance of individual regressors. We used Fisher's exact test in place of the generalized estimating equation when there were one or more zero frequencies in the two-way table defined by the categorical predictor and dichotomous outcome. All tests were two-tailed with alpha set at 0.05.

Results

Data for some children were missing because not all measures were collected for all children. For the 179 children of parents with both panic disorder and major depression, we had structured diagnostic interview data for 141 children and Child Behavior Checklist data for 150. For the 29 children of parents with panic disorder only, we had structured diagnostic interview data for 26 and Child Behavior Checklist data for 25. For the 59 children of parents with major depression only, we had structured diagnostic interview data for 46 and Child Behavior Checklist data for 50. For the 113 comparison children whose parents who had neither panic disorder nor major depression, we had structured diagnostic interview data for 99 and Child Behavior Checklist data for 101.

Among children providing structured interview data, 195 were age 5–6, 75 were age 7–9, and 42 were over age 9. Among children for whom Child Behavior Checklist data were available, 111 were age 2–3, and 215 were age 4–18. As shown in Table 1, no significant differences between the children from the four parental diagnostic groups were found for age, gender, or sibship size. There were significant differences among groups for intactness of family and socioeconomic status and a difference that approached significance for race/ethnicity. Therefore, all analyses were corrected for these three variables.

Psychiatric Disorders in Children

Significant differences were detected between children from the four parental diagnostic groups in the mean number of anxiety disorders: mean=0.25 (SD=0.7) in the comparison children, and mean=0.65 (SD=1.3), mean=0.85 (SD=1.5), and mean=1.0 (SD=1.5) in the children of parents with major depression only, panic disorder only, and both panic disorder and major depression, respectively ($\chi^2=19.3$, $df=3$, $p<0.001$). Children of all three groups of parents with psychopathology differed significantly from comparison children in the mean number of anxiety disorders ($z=2.35$, $p<0.02$; $z=2.60$, $p=0.009$; and $z=4.32$, $p<0.001$ for comparisons involving children of parents with major depression only, panic disorder only, and both panic disorder and major depression, respectively). Differences remained significant when demographic confounds were covaried.

Significant differences between groups were found for rates of multiple anxiety disorders (two or more anxiety disorders in the same child), separation anxiety disorder, agoraphobia, social phobia, panic disorder, and avoidant disorder (Figure 1). Although we found no significant differences among the children in various psychopathologic groups, each group showed some differences from the comparison children. Separation anxiety disorder and multiple anxiety disorders showed nonspecific effects inasmuch as the children of all three groups of parents with psychopathology showed significantly higher rates of

TABLE 1. Demographic Characteristics of Children in a Familial Study of Anxiety Disorders Whose Parents Had Both Panic Disorder and Major Depression, Panic Disorder Only, Major Depression Only, or Neither Disorder

Characteristic	Children of Parents With Both Panic Disorder and Major Depression (N=179)		Children of Parents With Panic Disorder Only (N=29)		Children of Parents With Major Depression Only (N=59)		Children of Parents Without Panic Disorder or Major Depression (N=113)		Analysis ^a		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Value	df	p
Age of child at interview (years)	6.8	2.8	6.6	1.5	6.7	2.5	6.8	1.9	F=0.2	3, 196	0.90
Parents' social class ^{b,c}	2.3	1.0	1.8	0.6	2.2	1.0	1.8	0.9	Wald $\chi^2=14.6$	3	0.002
Number of siblings in family	2.1	0.9	2.0	0.7	2.1	1.0	2.3	0.9	Wald $\chi^2=3.1$	3	0.39
	N	%	N	%	N	%	N	%	Value	df	p
Female child	85	47.5	13	44.8	23	39.0	46	40.7	Wald $\chi^2=2.1$	3	0.55
Intact family ^d	150	83.8	29	100.0	47	79.7	102	90.3			<0.02 ^e
Race/ethnicity											<0.06 ^{e,f}
Caucasian	171	95.5	29	100.0	54	91.5	100	88.5			
African American	5	2.8	0	0.0	3	5.1	4	3.5			
Hispanic	0	0.0	0	0.0	2	3.4	4	3.5			
Asian	3	1.7	0	0.0	0	0.0	5	4.4			

^a Associations tested by using a generalized estimating equation model controlling for intrafamilial clustering. Fisher's exact test used when one or more cells had a zero frequency.

^b Measured with the Hollingshead Four-Factor Index (34).

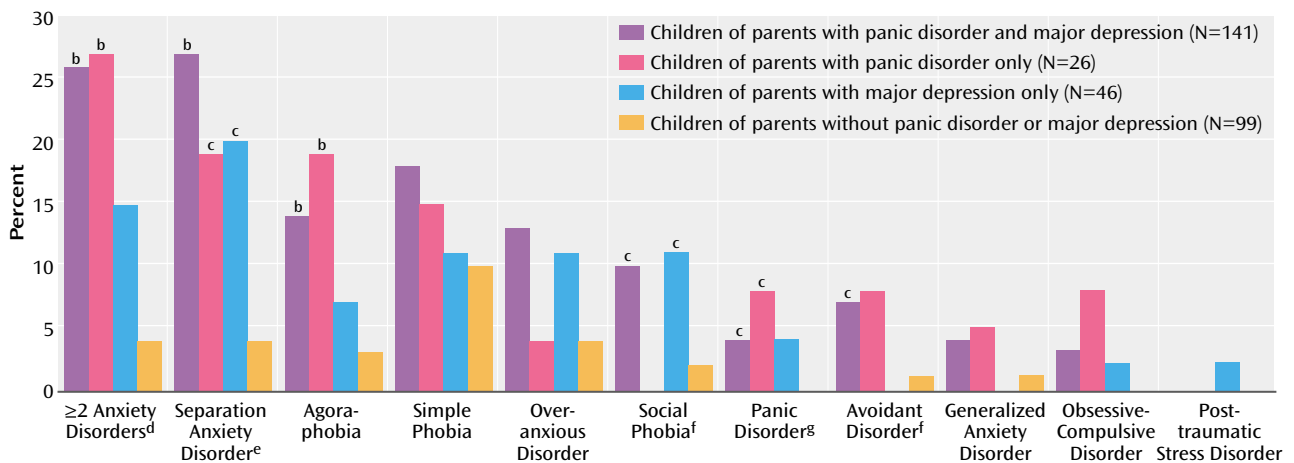
^c Significant differences between the panic-plus-depression group and the neither-disorder group (p<0.01), the panic-plus-depression group and the panic-only group (p<0.01), and the depression-only group and the neither-disorder group (p<0.05).

^d Significant differences between the panic-plus-depression group and the panic-only group (p<0.01), the depression-only group and the neither-disorder group (p<0.05), and the depression-only group and the panic-only group (p<0.01).

^e Fisher's exact test.

^f For comparison of Caucasian and non-Caucasian groups.

FIGURE 1. Rates of Individual and Multiple Anxiety Disorders in Children of Parents With Both Panic Disorder and Major Depression, Panic Disorder Only, Major Depression Only, or Neither Disorder^a



^a Associations tested by using the generalized estimating equation model controlling for intrafamilial clustering. Fisher's exact test used when one or more cells had a zero frequency.

^b Significantly different from children of parents with neither disorder (p<0.01).

^c Significantly different from children of parents with neither disorder (p<0.05).

^d Significant difference among groups (Wald $\chi^2=12.5$, df=3, p=0.006).

^e Significant difference among groups (Wald $\chi^2=13.4$, df=3, p=0.004).

^f Significant difference among groups (Fisher's exact test, p<0.03).

^g Significant difference among groups (Fisher's exact test, p<0.05).

those disorders than the comparison children. After covarying demographic confounds, the significant difference in the rate of multiple anxiety disorders between the children of parents with major depression and the compari-

son children became nonsignificant (odds ratio=4.0, 95% confidence interval [CI]=0.92–17.8, z=1.85, p=0.06).

In contrast, other disorders showed some evidence for specificity. Higher rates of panic disorder and agoraphobia

than in the comparison children were found only in children of parents with panic disorder and of parents with both panic disorder and major depression. Higher rates of social phobia than in comparison children were found only in children of parents with major depression and of parents with both panic disorder and major depression. After controlling for demographic confounds, the overall difference in the rates of agoraphobia between groups dropped to nonsignificance ($\chi^2=10.8$, $df=6$, $p<0.10$); however, the higher rates of agoraphobia in the children of parents with panic disorder (odds ratio=7.3, 95% CI=1.7–32.4, $z=2.63$, $p=0.009$) and in the children of parents with both panic disorder and major depression (odds ratio=5.5, 95% CI=1.6–19.0, $z=2.67$, $p=0.008$) retained significance. Although a higher rate of avoidant disorder was found in children of parents with panic disorder only and in children of parents with both panic disorder and major depression than in comparison children, the rate was significantly different only in the children of parents with both panic disorder and major depression.

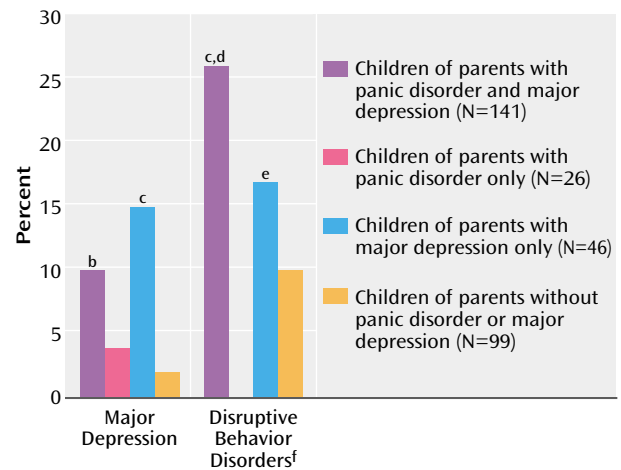
As shown in Figure 2, rates of major depression were significantly higher than in the comparison children among children of parents with major depression only and with both panic disorder and major depression but not among children of parents with panic disorder only. After controlling for demographic confounds, the overall difference in the rates of major depression between groups became nonsignificant ($\chi^2=11.2$, $df=6$, $p=0.08$); however, the higher rate in the children of parents with both panic disorder and major depression (odds ratio=5.1, 95% CI=1.1–24.4, $z=2.04$, $p<0.05$) and in the children of parents with major depression only (odds ratio=9.0, 95% CI=1.9–44.0, $z=2.72$, $p=0.006$) retained significance. A similar pattern was observed for disruptive behavior disorders, although the difference between the children of parents with major depression only and the comparison children failed to reach statistical significance (Figure 2).

The Child Behavior Checklist findings revealed significant differences among the groups in the frequency of scores indicating impairment (scores of 60 or higher) in scales measuring somatic problems (overrepresented in all high-risk groups); withdrawn, aggressive, and destructive behaviors (overrepresented in the children of parents with both panic disorder and major depression); and social interaction problems (overrepresented in children of parents with major depression only) (Figure 3). All comparisons retained significance when demographic confounds were covaried.

Psychosocial Functioning and Treatment in Children

We observed significant differences between groups on the Global Assessment of Functioning scale for both current and lifetime functioning (Table 2). Both the children of parents with major depression only and the children of parents with both panic disorder and major depression

FIGURE 2. Rates of Major Depression and Disruptive Behavior Disorders in Children of Parents With Both Panic Disorder and Major Depression, Panic Disorder Only, Major Depression Only, or Neither Disorder^a



- ^a Associations tested by using the generalized estimating equation model controlling for intrafamilial clustering. Fisher’s exact test used when one or more cells had a zero frequency.
- ^b Significantly different from children of parents with neither disorder ($p<0.05$).
- ^c Significantly different from children of parents with neither disorder ($p<0.01$).
- ^d Significantly different from children of parents with panic disorder only ($p<0.01$).
- ^e Significantly different from children of parents with panic disorder only ($p<0.05$).
- ^f Significant difference among groups (Fisher’s exact test, $p=0.001$).

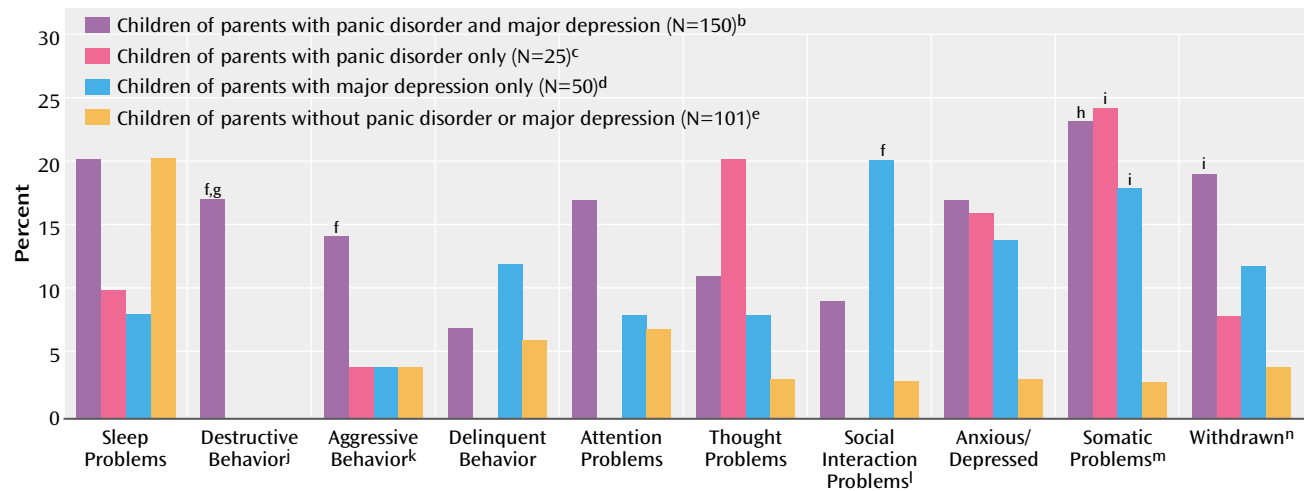
showed poorer levels of functioning than the comparison children. Although we observed a similar pattern for the total score of the Social Adjustment Inventory for Children and Adolescents, differences between groups became nonsignificant after covarying demographic confounds ($\chi^2=10.5$, $df=6$, $p=0.10$). As for school functioning, we found that the children of parents with both panic disorder and major depression had significantly higher frequencies of having repeated a grade than the comparison children. The groups did not differ in treatment history.

Discussion

Our results provide mixed support for the idea that the familial diathesis for anxiety disorders includes a nonspecific “anxiety proneness.” If that had been the case, we would have expected high rates of all anxiety disorders among children of parents with panic disorder. Instead, parental panic disorder, regardless of comorbidity with major depression, predicted child panic disorder and agoraphobia, but not other anxiety disorders. This finding confirms prior reports of a specific aggregation for panic disorder (10, 20, 21).

But we also found 1) that parental major depression, regardless of comorbidity with panic disorder, predicted increased risks for social phobia and major depression in children and 2) that both parental panic disorder and pa-

FIGURE 3. Rates of Impairment in Functional Areas Measured by the Child Behavior Checklist in Children of Parents With Both Panic Disorder and Major Depression, Panic Disorder Only, Major Depression Only, or Neither Disorder^a



^a T scores of ≥ 60 (i.e., one standard deviation above the mean) on the Child Behavior Checklist signified impairment. Responses for scales from both the version of the Child Behavior Checklist for 2–3-year-olds and the version for 4–18-year-olds were combined for this analysis. Data on sleep problems and destructive behavior are based on scales from the version for 2–3-year-olds; data on delinquent behavior, attention problems, thought problems, and social interaction problems are based on scales from the version for 4–18-year-olds; and data on the remaining variables are based on scales from both versions. Associations tested by using a generalized estimating equation model controlling for intrafamilial clustering. Fisher’s exact test used when one or more cells had a zero frequency.

^b For 2–3-year-olds, N=46; for 4–18-year-olds, N=104.

^c For 2–3-year-olds, N=10; for 4–18-year-olds, N=15.

^d For 2–3-year-olds, N=25; for 4–18-year-olds, N=25.

^e For 2–3-year-olds, N=30; for 4–18-year-olds, N=71.

^f Significantly different from children of parents with neither disorder ($p < 0.05$).

^g Significantly different from children of parents with major depression only ($p < 0.05$).

^h Significantly different from children of parents with neither disorder ($p < 0.001$).

ⁱ Significantly different from children of parents with neither disorder ($p < 0.01$).

^j Significant difference among groups (Fisher’s exact test, $p = 0.01$).

^k Significant difference among groups (Wald $\chi^2 = 9.0$, $df = 3$, $p = 0.03$).

^l Significant difference among groups (Fisher’s exact test, $p < 0.04$).

^m Significant difference among groups (Wald $\chi^2 = 13.9$, $df = 3$, $p = 0.003$).

ⁿ Significant difference among groups (Wald $\chi^2 = 9.8$, $df = 3$, $p = 0.02$).

rental major depression, individually or comorbidly, were associated with increased risk for separation anxiety disorder. This familial line between major depression and some anxiety disorders is consistent with prior studies (4, 5).

Our results indicate heterogeneity within the group of anxiety disorders. Some disorders may share a common familial vulnerability, others may be associated with the risk for major depression, and others may possibly represent nonspecific manifestations of risk in offspring of parents with anxiety or major depression. In our study, the risks for panic disorder and major depression were not additive. Having parents with two disorders did not double the child’s risk for having one. Instead, the pattern of risk was better predicted by which disorder had been diagnosed in the parent, regardless of the presence of other disorders. These findings stress the importance of considering specific anxiety disorders in studies of children at risk.

Equally consistent with the extant literature is our finding that separation anxiety disorder is associated with either anxiety or major depression in parents (40). This result, together with reports of others (41) failing to find

associations between adult panic or agoraphobia and childhood history of separation anxiety disorder, challenges the idea that separation anxiety disorder is a specific childhood antecedent of subsequent panic disorder or agoraphobia.

We also observed specificity of transmission of major depression between parents and children. Moreover, parental major depression increased the risk for major depression in the offspring irrespective of the presence of panic disorder in the parent. Similar findings have been reported by Weissman et al. (1). These findings suggest that there are separate familial vulnerabilities for panic disorder and major depression.

Notably, the risk for anxiety disorders in children of parents with panic disorder was not limited to the traditional childhood-onset disorders but also included the adult-type anxiety disorders panic disorder and agoraphobia. Although these adult-type disorders are not commonly assessed in pediatric studies, a body of literature has documented that these disorders occur and can be diagnosed in children (42, 43). Such findings support the value of considering the full spectrum of anxiety disorders in children.

TABLE 2. Functional Characteristics of Children of Parents With Both Panic Disorder and Major Depression, Panic Disorder Only, Major Depression Only, or Neither Disorder

Characteristic	Children of Parents With Both Panic Disorder and Major Depression			Children of Parents With Panic Disorder			Children of Parents With Major Depression			Children of Parents Without Panic Disorder or Major Depression			Analysis ^a	
	Total N	Mean	SD	Total N	Mean	SD	Total N	Mean	SD	Total N	Mean	SD	Wald χ^2 (df=3)	p
Social competence areas measured by the Child Behavior Checklist (T scores)														
Social relations	43	47.6	6.8	6	41.8	7.3	9	48.8	6.2	32	47.8	8.1	2.4	0.49
Activities	53	47.6	6.6	9	48.4	4.4	9	49.7	4.8	40	47.9	5.7	0.8	0.86
School functioning	36	46.2	8.2	7	45.0	7.8	8	46.9	6.8	28	48.1	7.6	3.2	0.36
Social Adjustment Inventory for Children and Adolescents score ^b														
Global Assessment of Functioning score	110	15.0	4.0	19	14.7	2.4	36	16.1	5.2	82	13.6	3.3	8.6	<0.04 ^c
Current (past month) ^d	141	65.6	7.7	26	68.3	5.0	46	66.8	5.9	99	69.8	4.0	29.4	<0.001
Lifetime (worst functioning) ^e	141	63.7	8.7	26	66.3	5.9	46	64.9	6.8	99	68.7	5.7	24.9	<0.001
School functioning														
Repeated grade ^f	141	9	6.4	26	1	3.8	46	1	2.2	99	0	0.0		<0.04 ^g
Needed tutoring	141	17	12.1	26	3	11.5	46	8	17.4	99	9	9.1	1.7	0.64
Placed in special class	141	8	5.7	26	1	3.8	46	3	6.5	99	4	4.0	0.5	0.91
Treatment history														
Counseling only	125	28	22.4	24	8	33.3	40	10	25.0	88	10	11.4	6.6	<0.09
Pharmacotherapy only	125	1	0.8	24	0	0.0	40	0	0.0	88	0	0.0		1.00 ^g
Counseling and pharmacotherapy	125	5	4.0	24	0	0.0	40	0	0.0	88	2	2.3		0.74 ^g
Psychiatric hospitalization	125	1	0.8	24	0	0.0	40	0	0.0	88	0	0.0		1.00 ^g

^a Associations tested by using a generalized estimating equation model controlling for intrafamilial clustering. Fisher's exact test used when one or more cells had a zero frequency.
^b Significant differences between the panic-plus-depression group and the neither-disorder group (p<0.05) and between the depression-only group and the neither-disorder group (p<0.05).
^c Overall difference became nonsignificant after demographic confounds (age, gender, socioeconomic status, size of sibship, intactness of family, and race/ethnicity) were covaried.
^d Significant differences between the panic-plus-depression group and the neither-disorder group (p<0.001), between the panic-plus-depression group and the panic-only group (p<0.05), and between the depression-only group and the neither-disorder group (p<0.01).
^e Significant differences between the panic-plus-depression group and the neither-disorder group (p<0.001) and between the depression-only group and the neither-disorder group (p<0.01).
^f Significant difference between the panic-plus-depression group and the neither-disorder group (p<0.01).
^g Fisher's exact test.

In addition to increasing the risks for major depression and anxiety disorders in the offspring, parental major depression also increased the risk for disruptive behavior disorders both as a diagnosis and as measured by the Child Behavior Checklist. This finding is consistent with literature documenting a high degree of syndromatic overlap and familial co-aggregation between disruptive behavior and depressive disorders (44–46).

Despite these differences in psychopathology among the groups, we found few differences in levels of functioning. The strongest differences were for both current and lifetime functioning on the Global Assessment of Functioning scale, on which children of parents with major depression only or with both panic disorder and major depression showed poorer levels of functioning than the comparison children. There were small differences on the total score of the Social Adjustment Inventory for Children and Adolescents, but these were accounted for by intactness of family, socioeconomic status, and race/ethnicity.

We found no differences on Child Behavior Checklist measures of functioning and only one sign of school dysfunction, more repeated grades among children of parents with both panic disorder and major depression. Consistent with the minimal differences in functioning, treatment history findings revealed no significant differences among groups.

The low levels of treatment are consistent with the findings of Weissman et al. (47), who reported that one-third of depressed high-risk children had not been treated during a 10-year follow-up period despite impaired family and work functioning. Moreover, epidemiologic studies have suggested that underidentification is pervasive; only a small fraction of youth with mental disorders receive adequate treatment (48). These results call for increased efforts to identify emotional and behavioral difficulties in children of parents referred for anxiety and depression to adult psychiatry practices.

Our findings should be viewed in the context of the study's methodological limitations. Any interpretation of these findings must be tempered by the fact that these children are still early in the risk period for anxiety and depressive disorders. Future onset of illness may lead to different inferences about patterns of transmission. The assessment of psychopathology in the children was based mainly on interviews with the mothers. Psychiatric disorders in parents may have affected the reported rates of childhood symptoms. Psychiatric patients may exaggerate symptoms in their children, or, alternatively, mothers without psychopathology may underreport problem behaviors (49). Another concern is that the numbers of parents with major depression only and with panic disorder only (without comorbid major depression) were relatively small and so did not afford adequate statistical power for a thorough test of associations between major depression or panic disorder in parents and in their high-risk children. Because we conducted multiple statistical tests without a Bonferroni correction, some of our findings may be due to chance. Had we used a Bonferroni correction, psychopathology findings would have been significant at $p < 0.004$ (Figure 1 and Figure 2), Child Behavior Checklist findings would have been significant at $p < 0.005$ (Figure 3), and functional characteristics at $p < 0.004$ (Table 2). Thus, our results should be viewed cautiously until confirmed in additional studies.

Because the proband parents were clinically referred, the generalizability of our findings is limited to offspring of referred patients. Also, the large majority of subjects were Caucasians from intact families and higher social classes. Further work is needed to determine if our results generalize beyond these constraints.

Despite these considerations, in a large group of children at risk we found that parental panic disorder and major depression conferred a significant risk for dysfunction and emotional distress in their offspring. A longitudinal follow-up of this group is needed to determine whether these difficulties will confer further vulnerability on these children as well as to identify risk and protective factors that influence the transition from childhood to adult anxiety disorders.

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