Children of Currently Depressed Mothers: A STAR*D Ancillary Study

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Objective: To assess the current and lifetime prevalence of psychiatric disorders among children of currently depressed mothers and to assess the association of clinical features of maternal depression (i.e., severity, chronicity, and clinical features) with child psychopathology. Mothers were participants in the STAR*D (Sequenced Treatment Alternatives to Relieve Depression) multisite trial, designed to compare effectiveness and acceptability of different treatment options for outpatients with nonpsychotic major depressive disorder (MDD).

Method: Treatment-seeking mothers with a current DSM-IV diagnosis of MDD and with at least 1 child 7 to 17 years old were assessed during a major depressive episode (MDE). For each mother, 1 child was assessed (if a mother had more than 1 child, 1 was randomly selected). Maternal features assessed for this study were history of MDEs, severity of current MDE, comorbid conditions, depressive symptom features, and social functioning. Children were assessed for selected psychiatric diagnoses (Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version [K-SADS-PL]), psychopathologic symptoms and social functioning (Child Behavior Checklist), and global functioning (Children's Global Assessment Scale). Data were gathered from December 2001 to April 2004.

Results: A large proportion (72%) of mothers were severely depressed (17-item Hamilton Rating Scale for Depression score ≥ 22). About a third (34%) of children had a current psychiatric disorder, including disruptive behavior (22%), anxiety (16%), and depressive (10%) disorders. Nearly half (45%) had a lifetime psychiatric disorder, including disruptive behavior (29%), anxiety (20%), and depressive (19%) disorders. Atypical depressive features in the mother were associated with a 3-fold increase in the odds of having a child with depressive (OR = 3.3 [95% CI = 1.2 to 9.5]; p = .02) or anxiety (OR = 2.6 [95% CI = 1.1 to 6.9]; p = .03) disorders. A history of maternal suicide attempts and the presence of comorbid panic disorder with agoraphobia were associated with a 3-fold increase and an 8-fold increase in the odds of depressive disorders in the offspring, respectively. The final model showed significant associations ($p \leq .05$) between the following characteristics of maternal depression and offspring disorders: maternal comorbid panic disorder with agoraphobia and offspring depressive and anxiety disorders, maternal irritable depression and offspring disruptive behavior disorders and any disorder, and maternal substance use disorders and any disorder.

Conclusions: Children of mothers in the midst of a current MDE are at high risk for disruptive behavior and anxiety disorders. The elevated risk of psychopathology among children of depressed mothers may recommend assessment of these children when clinically suggested. Children of depressed mothers with comorbid panic disorder with agoraphobia are at high risk for depressive and anxiety disorders and deserve special attention from clinicians.

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Major depressive disorder (MDD) is a highly prevalent, often familial disorder that frequently affects the young.[1] It results in significant social impairment, often leading to increased utilization of medical and mental health services.[2] The highest prevalence of MDD is found in women in their childbearing years,[3,4] and economically disadvantaged mothers are most vulnerable.[5]

Numerous studies have shown that offspring of depressed parents are at an over 2-fold increased risk of adult MDD, as well as other psychiatric disorders, and impaired social functioning.[6,7] Disorders in offspring vary by age: disruptive behavior and anxiety disorders in school-age children; depression in adolescents; and substance abuse in young adults, with depressive disorders continuing into adulthood and across several generations.[8] Previous studies of high risk children[6,8] focused on the lifetime prevalence of psychiatric disorders in the offspring of parents with a lifetime history of MDD. The present study focused on children of currently depressed mothers (in the midst of a current major depressive episode [MDE]) who sought treatment in psychiatric and primary care clinics. This study included a baseline assessment to ascertain the presence of psychiatric disorders and the degree and types of impairment seen in these children. A follow-up phase will determine whether a decrease of maternal depressive symptoms with treatment is accompanied by decreased psychiatric symptoms or improvement in social functioning in these children.

We examined the prevalence of both current and lifetime psychiatric disorders in children of these depressed mothers. Additionally, we studied associations between the clinical features of the maternal depression (i.e., severity, chronicity, clinical features, and comorbid psychiatric or general medical conditions) and children's psychopathology. Several studies have addressed the impact of chronicity and severity of maternal depression on the offspring of depressed mothers.[9–12] Brennan et al.[11] reported that both the severity and chronicity of maternal depressive symptoms assessed by self-report at 4 time intervals (pregnancy, postpartum, and when the child was 6 months and 5 years old) were associated with more behavior problems and lower vocabulary scores at age 5. Hammen and Brennan[12] reported that the severity of maternal depression contributed more to children's depression than did chronicity, but both made a contribution. We hypothesized that maternal depression severity and chronicity would be associated with a higher prevalence of depressive disorders in the offspring.

Comorbid disorders are present in about half of cases of MDD, with anxiety disorders being the most frequently associated condition.[13,14] The role of these maternal comorbid disorders in conferring risk to children has received minimal attention.[15] Children of depressed mothers with comorbid disorders participating in the Yale family study of depression[16] were more likely to have depressive or anxiety disorders. Lifetime maternal comorbid panic and agoraphobia were associated with a markedly increased prevalence of MDD in the offspring (13.2% in children of mothers with MDD alone, 22.2% for depression and agoraphobia, and 26.3% for depression and panic).[16] Four-month-old infants of mothers with a lifetime history of depression and comorbid conditions (anxiety, substance, and eating disorders) had less optimal play interactions than infants of women with depression without comorbid psychopathology.[15] One report found that comorbid parental panic disorder and major depression were associated with increased risk for separation anxiety disorder and multiple (2 or more) anxiety disorders in offspring.[17]

We hypothesized that children of depressed mothers with concurrent comorbid Axis I disorders would have a higher prevalence of psychiatric disorders, as compared with children of mothers with uncomplicated depression (i.e., without comorbidity), and that current comorbid anxiety disorders in depressed mothers would increase the odds of anxiety disorders in their children.

METHOD

Sample

Mothers were enrolled as participants in a large study focusing on the treatment of adult outpatients with nonpsychotic MDD, known as STAR*D (Sequenced Treatment Alternatives to Relieve Depression).[18,19] We initiated the present multisite study known as STAR*D Child to assess the impact on children of improvement or remission of maternal depression. Data were gathered from December 2001 to April 2004.

STAR*D trial. STAR*D is a multisite study designed to determine the comparative effectiveness and acceptability of different treatment options for a broadly representative group of outpatients with nonpsychotic MDD. Clinical sites included primary and specialty care settings serving public or private sector patients. STAR*D participants include adults, aged 18 to 75 years, with nonpsychotic MDD and without a lifetime diagnosis of bipolar, schizophrenia, or schizoaffective disorders. Patients with concurrent medical and psychiatric conditions, except as noted above, were included. STAR*D offers 5 treatment levels delivered sequentially and described in detail elsewhere.[18,19] At the outset, all study participants were initially treated with citalopram (Level I treatment). Those not remitting with citalopram could receive subsequent treatment steps provided in a randomized design. Seven of the 14 STAR*D Regional Centers participated in STAR*D Child.

STAR*D Child trial. Women aged 25 to 60 years entering STAR*D at 1 of the 7 participating regional centers were screened to ascertain whether they had age-eligible children. Eligible mothers for STAR*D Child had to have at least 1 child aged 7 to 17 years. They were invited to participate in STAR*D Child, with 1 of their eligible children, and they provided a separate written informed consent. Children living with their mothers (or in case of marital separation or divorce, living with her at least 50% of the time) were eligible unless they suffered from conditions that could interfere with their ability to comprehend study

assessments (e.g., severe mental retardation, pervasive developmental disorders). If a mother had more than 1 child aged 7 to 17 years, 1 was selected using a table of random numbers.

STAR*D had recruited 824 women aged 25 to 60 years at regional centers participating in the STAR*D Child study; 808 (98%) of these women were screened to ascertain that they had at least 1 child aged 7 to 17 years; 177 (22%) of them had children in that range; of these, 174 (98%) met all eligibility criteria; of these, 151 mother-child pairs (87%) consented to participate in the STAR*D Child trial. This report includes all 151 pairs.

Mothers and children were assessed before the initiation of treatment or before they could be expected to benefit from treatment (i.e., within 2 weeks following the initiation of treatment with citalopram). Because maternal reports of children's clinical status can be influenced by mothers' depression, we obtained information from both mothers and children.[20]

Assessments and Measures

The present report is based on the baseline assessments of mothers, including assessments conducted as part of the STAR*D study, and assessments of mothers and their children as part of the STAR*D Child study.

Mothers. Mothers received a comprehensive battery of assessments.[18,19] In addition, the mothers completed the Social Adjustment Scale Self-Report (SAS-SR) as part of the STAR*D Child study. The STAR*D maternal assessments were obtained by clinical research coordinators as detailed elsewhere.[19] Assessments relevant to this report include the following:

Diagnosis. A diagnosis of a current single or recurrent nonpsychotic major depressive disorder was established by clinical interview and confirmed using a symptom checklist based on DSM-IV criteria.[21]

Hamilton Rating Scale for Depression. This clinician-rated scale is widely used to assess the severity of depressive symptoms.[22,23] The Hamilton Rating Scale for Depression ($HAM\text{-}D_{17}$) has good reliability, and scores are highly correlated with the results from other observer-rated instruments.[24] Maternal depression status for all 151 mothers was classified as either moderate ($HAM\text{-}D_{17}$ score of 14–21) or severe ($HAM\text{-}D_{17}$ score ≥ 22), using thresholds similar to those reported in the literature.[25,26]

Demographic and clinical assessment. As part of the STAR*D assessment, demographic and clinical information was collected, including a history of MDEs and of suicide attempts. Maternal concurrent psychiatric (Axis I) disorders were determined using the Psychiatric Diagnostic Screening Questionnaire (PDSQ), as previously described,[27] set at 90% specificity.[28] Mothers also completed the 30-item Inventory of Depressive Symptomatology-Clinician Rating ($IDS\text{-}C_{30}$).[29–31]

Characteristics of maternal depression considered in this study include age of mother at first MDE, whether the first MDE began prior to 18 years of age, the number of MDEs, length and severity of current MDE (as assessed using the $HAM\text{-}D_{17}$, described above), years of child exposure to maternal MDD (defined as the period between the first onset of maternal MDD and the baseline evaluation, except when the mother's first onset of MDD preceded the birth of the child, in which case the period of exposure was equal to the child's age), the average number of MDEs per year of exposure to maternal MDD, and whether the mother had a lifetime history of suicide attempts (yes/no). We also examined the presence of concurrent maternal comorbid conditions, another indicator of severity of the overall clinical condition of the mother, based on the PDSQ.[27] We further classified the clinical features of maternal depression (current MDE) using items from the $HAM\text{-}D_{17}$ and the $IDS\text{-}C_{30}$, as explained elsewhere, into 4 categories: atypical,[32] anxious,[33] melancholic,[34] or irritable[35] depression. These data were used in the present study to examine associations between the clinical features of maternal depression and child psychopathology.

Social Adjustment Scale Self-Report. The SAS-SR is a reliable and widely used assessor of 6 major areas of social functioning: work (which includes employment, housework, and student work), social and leisure activities, relationships with extended family, primary relationship, parental role, and role within the family unit.[36] The current study assessed all domains except relationships with extended family. A higher SAS-SR score is indicative of greater functional impairment.

Children. Children's psychiatric disorders were established using the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL).[37] Global functioning was assessed using the Children's Global Assessment Scale (C-GAS),[38] and competencies and psychopathologic symptoms were assessed using the Child Behavior Checklist (CBCL).[39]

Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version. The K-SADS-PL is a valid and reliable diagnostic instrument that generates DSM-IV psychiatric diagnoses. Test-retest reliability kappa coefficients are in the good-to-excellent range (0.63 to 1.00) for present and/or lifetime diagnoses.[37] To avoid overburdening participants, we selected sections of the K-SADS-PL targeting disorders known to be highly prevalent among children of depressed parents[6,40]: affective, anxiety, and disruptive behavior disorders.

Children's Global Assessment Scale. The C-GAS, a clinician-rated measure of global functioning, was developed by Shaffer et al.[38] It has been shown to be reliable between raters and across time, with demonstrated discriminant and concurrent validity. The C-GAS provides a good

estimate of overall severity of disturbance (range, 0–100). Scores above 90 indicate superior functioning, and scores below 70 indicate impaired global functioning.

Child Behavior Checklist. The CBCL is a highly reliable and widely used parent-rated checklist to assess competencies and behavioral and emotional problems in children 4 to 18 years of age.[39] The CBCL includes 3 social functioning competencies: activities, socialization, and school functioning (range, 0–100). All scores presented here are normalized scores (T scores). Higher competence scores indicate better social functioning; scores lower than 30 are considered in the clinical range. The CBCL also yields an overall psychopathology score composed of 2 domains: internalizing and externalizing symptoms (range, 0–100). Higher psychopathology scores reflect more (or more severe) symptoms, and scores above 70 are considered in the clinical range.

Qualifications, Training of Interviewers, and Reliability

Diagnostic assessments of children (K-SADS-PL) were performed by experienced master's- or doctoral-level mental health professionals who completed a 2-day training program. Their ratings of a videotaped interview were compared with those of one of the authors (D.J.P.) at the completion of training. The mean kappa for agreement on symptoms at training completion was 0.79.

Quality Assurance

Quality assurance activities included monthly conference calls to discuss protocol adherence, site visits to ascertain compliance with the protocol, and periodic assessments of diagnostic reliability conducted by obtaining audiotapes or videotapes of interviews done at the sites and comparing the diagnoses with those made by one of the authors (D.J.P.). The mean kappa for agreement across diagnoses was 0.87.

Data Analysis

All statistical analyses were conducted in Statistical Analysis System (SAS) 12.0 (SAS; Cary, N.C.). Comparisons of children's diagnoses by severity of maternal depression were made using logistic regression analysis, with child diagnosis as a dichotomous outcome, mother's depression status (moderate/severe) as the independent variable, and age and gender of child included as potential confounding variables. Fisher exact tests were used when there were no children with a particular diagnosis for a particular maternal depression category. Comparisons of children's CBCL competency and psychopathology scores were made using linear regression models with the children's competency or psychopathology scores as the continuous dependent variable and mothers' depression status (moderate/severe) as the independent variable of interest, with age and gender of child as covariates.

Comparisons of demographic characteristics of mothers by clinical setting (primary care vs. psychiatric settings) were made using t tests for continuous outcomes and χ^2 tests for dichotomous outcomes. For cumulative models shown in Table 5, a stepwise logistic regression function was used, and covariates significant at the $p \leq .05$ level of significance were verified using forward and backward regression functions and multivariate models incorporating these variables.

RESULTS

Maternal Characteristics

Participating mothers were moderately to severely depressed (mean HAM-D_{17} score = 24.7 [SD = 5.0]). Most mothers (N = 109; 72%) were severely depressed (HAM-D_{17} score ≥ 22), and the remaining mothers (N = 42; 28%) were moderately depressed (HAM-D_{17} score of 14–21). Mean HAM-D_{17} scores were not significantly different across the 7 sites of the study (range, 22.9 [SD = 4.0] to 26.0 [SD = 6.1]). Demographic characteristics of mothers and children are shown in Table 1.

Twenty-four mothers (16%) had specified clinical features of atypical depression (mean HAM-D_{17} score = 26.0 [SD = 5.1]); 80 (53%), of anxious depression (26.8 [4.7]); 28 (18%), of melancholic depression (27.9 [5.1]); and 92 (61%), of irritable depression (25.9 [4.6]). Thirty-five mothers (24%) had none of these 4 specified clinical features of depression (21.6 [4.3]). Mothers with 1 or more of the above specified clinical features of depression had higher HAM-D_{17} scores than mothers with no specified clinical features ($p < .01$). Forty-five mothers had 2 of the above clinical features (mean HAM-D_{17} score = 26.2 [SD = 4.7]), 27 mothers had 3 of the features (27.1 [4.6]), and 4 mothers had all 4 features of depression (31.5 [5.6]).

As assessed with the SAS-SR, mothers with severe depression, as compared to those with moderate depression, had greater impairment of social functioning in the following domains: primary relationship (mean score = 2.5 vs. 2.2; $p = .05$), family unit (2.6 vs. 2.1; $p = .006$), social and leisure activities (2.8 vs. 2.6; $p = .04$), and work (2.3 vs. 1.7; $p = .007$). However, differences in social functioning among mothers were not associated with rates of DSM-IV diagnoses or severity of symptoms in their children. Mothers receiving treatment in primary care tended to have lower household income than those receiving treatment in psychiatric settings (71% vs. 43% with an annual income below $40,000; $p = .08$) and were more likely to be on public assistance (38% vs. 13%; $p = .001$). However, after controlling for household income, a comparison of diagnoses among children of depressed mothers receiving treatment in these settings revealed no significant differences between the settings (data not shown).

Table 1. Characteristics of Mothers and Children Participating in STAR*D Child[a]

Characteristic	Value
Mothers (N = 151)	
Age, mean (SD), y	37.1 (6.6)
Ethnicity	
White	67 (44)
Black	56 (37)
Hispanic[b]	22 (15)
Other[c]	6 (4)
Marital status	
Married, living with husband	64 (42)
Single/divorced/separated	87 (58)
Employment status	
Employed full or part time	98 (65)
Homemaker	20 (13)
Student/unemployed	31 (21)
Education	
Some high school or less	21 (14)
High school graduate	29 (19)
Some college	69 (46)
College graduate and above	32 (21)
Receiving public assistance	43 (29)
Annual household income	
Under $14,999	38 (27)
$15,000–$39,999	58 (40)
$40,000 and above	49 (33)
Children (N = 151)	
Age, mean (SD), y	11.5 (2.8)
Girls	72 (48)
School	
Grades 1–6	81 (54)
Grades 7–12	68 (45)
Remedial class	23 (16)
Living with	
Biological mother only	72 (47)
Both biological parents	48 (32)
Other[d]	31 (21)

[a]Values shown as N (%) unless otherwise noted. Ns vary due to missing data.
[b]Mothers who identified themselves as Hispanic were excluded from all other categories.
[c]Includes 2 Asians, 1 American Indian, 1 Hawaiian, and 2 mothers who identified themselves as more than 1 race.
[d]Includes 25 children living with their biological mother and stepfather.
Abbreviation: STAR*D = Sequenced Treatment Alternatives to Relieve Depression.

Children's Diagnoses

Table 2 shows children's current and lifetime psychiatric diagnoses. About a third (34%) were diagnosed with a current psychiatric disorder at the time of the baseline evaluation. The rates for current disruptive behavior, anxiety, and depressive disorders were 22%, 16%, and 10%, respectively. Disruptive behavior disorders tended to be more prevalent in boys than in girls (28% vs. 15%, p = .06).

As shown in Table 2, 45% of children received a lifetime psychiatric diagnosis, including disruptive behavior (29%), anxiety (20%), and depressive disorders (19%). Whereas most anxiety and disruptive behavior disorders (86%–100%) had a preadolescent onset (age < 12 years), only 59% of depressive disorders were first diagnosed prior to adolescence. The age at onset was higher for depressive disorders than for either anxiety (p = .004) or disruptive behavior (p = .027) disorders.

Children's Global Functioning, Symptoms, and Comorbidity

The mean C-GAS scores were as follows: current functioning, 69.5 (SD = 12.7); most impaired lifetime functioning, 61.9 (SD = 11.4); and highest past functioning within the last year, 74.0 (SD = 11.9). Mean social competencies, as assessed using the CBCL, were as follows: activities, 43 (SD = 7); social, 42 (SD = 9); and school, 47 (SD = 8). The mean CBCL internalizing and externalizing scores were 55.5 (SD = 10.4) and 53.4 (SD = 10.6), respectively. After adjusting for age and gender, CBCL competency and psychopathology scores, as well as DSM-IV diagnoses, did not vary significantly among children of moderately and severely depressed mothers or across the 7 study sites.

As shown in Table 3, comorbid disorders were highly prevalent among children of depressed mothers. Forty percent of children with a current depressive disorder were also diagnosed with a concurrent anxiety disorder, and 58% of children with a current anxiety disorder were also diagnosed with a concurrent disruptive behavior disorder. These high rates of comorbidities were independent of child age and gender and severity of maternal depression (data not shown).

Associations With Features of Maternal Depression

There was no significant relationship between either lifetime or current prevalence of children's diagnoses and severity or chronicity of maternal depression, as assessed by (1) age of first maternal MDE, including whether or not the mother was 18 years or older at that first episode; (2) number of maternal MDEs; (3) length or severity of current MDE (assessed using the HAM-D_{17}); (4) total length of maternal depression; (5) years of child exposure to maternal depression (see Method); or (6) number of MDEs per year of exposure to maternal depression (data not shown). However, as shown in Table 4, clinical features of maternal depression had a discernable impact on children's disorders. Maternal depression with atypical features was associated with increased odds of offspring depressive (OR = 3.3, p = .02) and anxiety (OR = 2.6, p = .03) disorders. Maternal irritable depression was associated with increased odds of offspring disruptive behavior disorders (OR = 2.3, p = .03).

Several maternal concurrent Axis I comorbidities were also associated with a higher prevalence of childhood disorders (Table 4). Notably, comorbid panic disorder with agoraphobia was associated with an 8-fold increase in the odds of offspring depression (OR = 8.4 [95% CI = 2.5 to 29], p = .0006) and a 4-fold increase in the odds of offspring anxiety disorders (OR = 3.5 [95% CI = 1.5 to

Table 2. Current and Lifetime Prevalence and Odds of Children's Psychiatric Disorders According to Age at Onset and Gender (N = 151)[a]

	Current Diagnoses, N (%)			Boys vs Girls		Lifetime Diagnoses, N (%)		
Disorder	All Children	Boys (N = 79)	Girls (N = 72)	OR[b]	p	All Children	Age at Onset < 12 y[c]	Age ≥ 12 y[c]
Any depressive disorder	15 (10)	10 (13)	5 (7)	1.9	.25	28 (19)	17 (61)	11 (39)
Major depressive disorder	8 (5)	5 (6)	3 (4)	1.5	.56	15 (10)	9 (60)	6 (40)
Other depressive disorders[d]	7 (5)	5 (6)	2 (3)	2.4	.43	14 (9)	9 (64)	5 (36)
Any anxiety disorder	24 (16)	13 (17)	11 (15)	1.1	.8	30 (20)	30 (100)	0
Specific phobia	15 (10)	9 (12)	6 (8)	1.4	.53	18 (12)	18 (100)	0
Separation anxiety disorder	7 (5)	4 (5)	3 (4)	1.2	.79	13 (9)	13 (100)	0
Social phobia	8 (5)	3 (4)	5 (7)	0.5	.39	8 (5)	7 (88)	0
Other anxiety disorders[e]	5 (4)	3 (4)	2 (3)	1.4	.73	7 (5)	6 (86)	1 (14)
Any disruptive behavior disorder	33 (22)	22 (28)	11 (15)	2.1	.06	43 (29)	39 (91)	4 (9)
ADHD	26 (17)	18 (23)	8 (12)	2.4	.06	33 (22)	33 (100)	0
Oppositional defiant disorder	10 (7)	7 (9)	3 (4)	2.2	.25	15 (10)	13 (87)	2 (13)
Conduct disorder	2 (1)	1 (1)	1 (1)	0.9	.94	3 (2)	3 (100)	0
Adjustment disorders without depression[f]	2 (1)	1 (1)	1 (1)	0.9	.94	3 (2)	3 (100)	0
Any disorder	52 (34)	32 (41)	20 (28)	1.7	.1	68 (45)	56 (82)	11 (16)

[a]Ns vary due to missing data.
[b]Odds of receiving a specified diagnosis for male compared with female children (OR = 1.0).
[c]When there was more than 1 episode of a disorder, the onset of the first episode was considered the age at onset.
[d]Includes depressive disorder NOS, adjustment disorder with depressed mood, and adjustment disorder with mixed anxiety and depressed mood.
[e]Includes generalized anxiety disorder, obsessive-compulsive disorder, and anxiety disorder NOS.
[f]Adjustment disorder with anxiety, adjustment disorder with disturbance of conduct, adjustment disorder with mixed disturbance of emotion and conduct, and unspecified adjustment disorder.
Abbreviations: ADHD = attention-deficit/hyperactivity disorder, NOS = not otherwise specified.

Table 3. Current and Lifetime Comorbidity in Children of Depressed Mothers (N = 151)

Psychiatric Disorder	N	Any Depressive Disorder, N (%)	Any Anxiety Disorder, N (%)	Any Disruptive Behavior Disorder, N (%)
Current		Concurrent Comorbid Diagnoses		
Any depressive disorder	15	…	6 (40)	4 (27)
Any anxiety disorder	24	6 (25)	…	14 (58)
Any disruptive behavior disorder	33	4 (12)	14 (42)	…
Lifetime		Lifetime Comorbid Diagnoses		
Any depressive disorder	28	…	14 (50)	10 (36)
Any anxiety disorder	30	6 (20)	…	20 (67)
Any disruptive behavior disorder	43	10 (23)	20 (47)	…

10.9], p = .01), after controlling for child age and gender and maternal depression severity (HAM-D_{17} score). As shown in Table 4, maternal substance use disorders and history of lifetime suicide attempts (1 or more) were also associated with a 3-fold increase in the odds of offspring depressive disorders. Maternal family history (parent or sibling only) of MDD was also significantly associated with childhood depressive disorders (OR = 3.1 [95% CI = 2.1 to 5.9], p = .03), after controlling for child age and gender and maternal depression severity (HAM-D_{17} scores) (data not shown).

To ascertain the relative impact of severity, chronicity, and clinical features of maternal depression, as well as Axis I comorbidities and suicide history, on child psychopathology, the variables in Table 4 were incorporated within stepwise logistic regression models (see Method). Child disorders were the dichotomous outcome variables, and the maternal depression features, comorbid conditions, and suicide attempts (as indicated in Table 4), as well as child age and gender and maternal depression severity (HAM-D_{17}), were the independent covariates. Independent variables that fit the model at the $p \leq .05$ level of significance are shown in Table 5. Two findings are noteworthy. First, maternal panic disorder with agoraphobia predicted both child depressive (OR = 7.9 [95% CI = 2.4 to 25.9], p = .0006) and anxiety (OR = 3.9 [95% CI = 1.3 to 11.7], p = .01) disorders. Second, maternal irritable features (OR = 2.1 [95% CI = 1.1 to 4.2], p = .04) and substance use (drug or alcohol) disorders (OR = 3.2 [95% CI = 1.1 to 9.6], p = .03) were most strongly associated with any child disorders. Identical predictors with similar levels of significance were obtained using forward or backward regression models. The number of maternal Axis I comorbid disorders (from 0–10, as listed in Table 4) did not significantly impact childhood disorders, although children of mothers with a greater number of comorbidities tended to be more likely to have a depressive disorder after controlling for child age and gender and maternal HAM-D_{17} score (data not shown).

DISCUSSION

This study assessed children of currently depressed mothers and found a high rate of psychopathology in their children (34% and 45% with a current and a lifetime

Table 4. Adjusted Odds[a] and Proportion (%) of Children With Lifetime Psychiatric Disorders According to Characteristics of Maternal Depression[b]

	Child Lifetime Psychiatric Disorder							
	Any Depressive Disorder		Any Anxiety Disorder		Any Disruptive Behavior Disorder		Any Disorder	
Maternal Illness Characteristic	N (%)	Adjusted OR (95% CI)	N (%)	Adjusted OR (95% CI)	N (%)	Adjusted OR (95% CI)	N (%)	Adjusted OR (95% CI)
Type of depression								
Atypical								
Yes (N = 24)	8 (33)	3.3 (1.2 to 9.5)*	9 (38)	2.6 (1.1 to 6.9)*	6 (25)	0.7 (0.3 to 2.1)	12 (50)	1.2 (0.5 to 2.9)
No (N = 124)	20 (16)		21 (17)		37 (30)		56 (45)	
Anxious								
Yes (N = 80)	17 (21)	14 (0.5 to 3.7)	15 (19)	0.6 (0.2 to 1.9)	28 (35)	2.1 (0.8 to 4.7)	42 (53)	1.8 (0.9 to 3.6)
No (N = 69)	11 (16)		15 (22)		15 (22)		26 (38)	
Melancholic								
Yes (N = 28)	4 (14)	0.7 (0.2 to 2.3)	3 (11)	0.2 (0.1 to 1.1)	9 (32)	0.9 (0.4 to 2.4)	13 (46)	1.0 (0.4 to 2.5)
No (N = 121)	24 (20)		27 (22)		35 (29)		55 (45)	
Irritable								
Yes (N = 92)	20 (21)	1.9 (0.7 to 4.9)	20 (22)	1.1 (0.4 to 2.6)	32 (35)	2.3 (1.1 to 5.5)*	48 (52)	2.1 (1.1 to 4.5)*
No (N = 57)	8 (14)		10 (18)		11 (19)		20 (35)	
Comorbid conditions[c]								
GAD								
Yes (N = 42)	7 (16)	1.0 (0.35 to 2.84)	13 (31)	2.0 (0.8 to 4.9)	12 (29)	0.9 (0.4 to 2.2)	20 (48)	1.1 (0.5 to 2.5)
No (N = 107)	21 (20)		17 (15)		31 (29)		48 (45)	
Social phobia								
Yes (N = 67)	14 (21)	1.5 (0.6 to 3.7)	14 (21)	1.0 (0.4 to 3.6)	17 (25)	0.6 (0.3 to 1.4)	28 (42)	0.7 (0.4 to 1.4)
No (N = 82)	12 (15)		15 (18)		25 (30)		38 (46)	
Bulimia nervosa								
Yes (N = 22)	5 (23)	1.7 (0.5 to 5.3)	6 (27)	1.4 (0.4 to 4.1)	6 (27)	0.8 (0.2 to 2.4)	12 (54)	1.6 (0.6 to 4.1)
No (N = 125)	21 (17)		23 (18)		36 (29)		54 (43)	
OCD								
Yes (N = 31)	6 (19)	1.1 (0.3 to 3.7)	8 (26)	1.2 (0.4 to 3.3)	11 (35)	1.5 (0.6 to 3.5)	18 (58)	1.9 (0.8 to 4.7)
No (N = 118)	22 (19)		22 (19)		32 (27)		50 (42)	
PTSD								
Yes (N = 26)	8 (31)	2.5 (0.8 to 7.7)	5 (19)	0.6 (0.2 to 2.2)	5 (19)	0.4 (0.1 to 1.1)	14 (54)	1.1 (0.4 to 2.9)
No (N = 121)	18 (15)		24 (20)		37 (31)		52 (43)	
Panic disorder without agoraphobia								
Yes (N = 15)	5 (33)	2.9 (0.7 to 11.0)	3 (20)	0.7 (0.1 to 2.9)	1 (6)	0.1 (0.01 to 0.9)	7 (47)	0.8 (0.3 to 2.8)
No (N = 132)	21 (16)		26 (20)		41 (31)		59 (45)	
Panic disorder with agoraphobia								
Yes (N = 16)	8 (50)	8.4 (2.5 to 29)**	7 (44)	3.5 (1.5 to 10.9)*	4 (25)	0.7 (0.2 to 2.4)	10 (63)	2.9 (0.7 to 6.2)
No (N = 130)	8 (6)		21 (16)		37 (29)		55 (42)	
Substance use disorder[d]								
Yes (N = 17)	6 (35)	3.4 (1.2 to 9.8)*	6 (35)	2.0 (0.7 to 5.7)	8 (47)	1.8 (0.7 to 4.8)	12 (70)	3.2 (1.1 to 9.6)*
No (N = 132)	22 (17)		24 (18)		35 (27)		56 (42)	
Hypochondriasis								
Yes (N = 8)	1 (12)	0.8 (0.09 to 7.6)	2 (25)	1.0 (0.1 to 5.5)	3 (38)	1.5 (0.3 to 7.1)	3 (38)	0.7 (0.1 to 3.3)
No (N = 139)	25 (18)		27 (19)		39 (28)		63 (35)	
Somatoform disorder								
Yes (N = 9)	2 (22)	1.4 (0.2 to 7.8)	3 (33)	1.9 (0.4 to 8.3)	4 (44)	2.0 (0.5 to 8.2)	4 (44)	0.9 (0.2 to 3.8)
No (N = 138)	24 (17)		26 (19)		38 (28)		62 (45)	
Attempted suicide (lifetime)								
Yes (N = 42)	12 (29)	2.9 (1.2 to 7.7)*	9 (21)	0.8 (0.3 to 1.9)	12 (29)	1.0 (0.4 to 2.2)	20 (48)	1.2 (0.6 to 2.5)
No (N = 109)	16 (15)		21 (19)		31 (28)		48 (44)	

[a]Adjusted for children's gender and age and maternal depression severity (17-item Hamilton Rating Scale for Depression scores). The comparison group (OR = 1.0) is all mothers without a disorder or factor. For example, in the case of maternal atypical depression, the comparison group is mothers without atypical depression.
[b]Ns vary due to missing data.
[c]Assessed using the Psychiatric Diagnostic Screening Questionnaire (see Method).
[d]Includes either drug or alcohol abuse or dependence.
*$p < .05$.
**$p < .01$.
Abbreviations: GAD = generalized anxiety disorder, OCD = obsessive-compulsive disorder, PTSD = posttraumatic stress disorder.

Table 5. Characteristics of Maternal Depression Associated With Children's Psychiatric Disorders

Predictor of Child Psychiatric Disorder	Adjusted OR (95% CI)[a]	p
Any child depressive disorder		
Maternal panic disorder with agoraphobia	7.9 (2.4 to 25.9)	.0006
Child age	1.3 (1.1 to 1.5)	.008
Any child anxiety disorder		
Maternal panic disorder with agoraphobia	3.9 (1.3 to 11.7)	.01
Any child disruptive behavior disorder		
Maternal irritable depression	2.6 (1.5 to 6.1)	.02
Any child disorder		
Maternal irritable depression	2.1 (1.1 to 4.2)	.04
Maternal substance use disorder	3.2 (1.1 to 9.6)	.03

[a]Stepwise logistic regression models using maternal types of depression, comorbid diagnoses, and attempted suicides as dichotomous independent variables, child outcomes (depressive, anxiety, and disruptive behavior disorders) as dichotomous dependent variables, and children's demographic characteristics (age and gender) as control variables.

psychiatric disorder, respectively). Thus, this study shows that about a third of children had significant problems while their mothers were in the midst of an MDE.

The high lifetime prevalences of psychiatric disorders in these children should be viewed in the context of this specific sample, which includes only depressed treatment-seeking mothers (children were assessed while their mothers were in the midst of a current MDE). Most of these mothers (72%) were severely depressed (HAM-D_{17} score ≥ 22), and many were living in poverty (29% receiving public assistance). There were no statistically significant differences in the lifetime prevalence of children's psychiatric disorders (K-SADS-PL) or symptoms (CBCL) according to the severity of maternal depression. However, because the sample included only untreated and mostly severely depressed mothers, the variability in the severity of maternal depression, as assessed using HAM-D_{17} scores, was limited. Because previous studies included parents (or mothers) with a lifetime history of MDD,[6,8] the parents may or may not have been depressed when their children were assessed.

Most of the anxiety and disruptive behavior disorders in these children had a prepubertal onset, a pattern similar to that noted in our previous studies of children of depressed parents.[40,41] Those studies also showed that depression had an adolescent onset. In the present study, although the mean age at onset for depressive disorders was significantly higher than those for anxiety and disruptive behavior disorders, adolescent-onset MDD (age ≥ 12 years) was somewhat less frequent than preadolescent-onset MDD (age < 12 years), perhaps due to the fact that this is a young sample (mean age = 11.5 years) and most children had not gone through the entire period of high risk for MDD (adolescence and early adult years).

The pattern of comorbidity noted in this study is similar to that shown in our previous studies of children of depressed parents[8] and to that shown in clinical samples of depressed children,[42,43] although, as expected, it exceeds that reported in community samples. For example, among high school students with depression, Lewinsohn et al.[44] reported that 21% and 12% had lifetime comorbid anxiety and disruptive behavior disorders, respectively. In contrast, in the present study, 50% and 31% of children with a lifetime depressive disorder had lifetime comorbid anxiety and disruptive behavior disorders, respectively.

Seventy-four children (49%) and 112 children (74%) had C-GAS scores below 70 for current and most severely impaired functioning, respectively. Scores below 70 are indicative of disorder severity and predictive of treatment outcomes.[45,46] Thus, nearly half (49%) of the children were significantly impaired at baseline. CBCL competency and psychopathology scores were not in the clinically impaired range, but reflected lower competencies and greater impairment than were observed in a large sample of nonreferred children in the community.[39]

The indicators of chronicity of maternal depression examined, i.e., age at first MDE, length of illness for MDD, years of child exposure to maternal MDD, and number of MDEs per year of exposure, were not associated with children's outcomes. Whereas some studies[11,47,48] have found a significant relation between chronicity of maternal depression and child outcomes, others[9,12,49] have reported a link between severity of maternal depression and child functioning. The study by Hammen and Brennan[12] suggested that severity of maternal depression is more likely to be associated with offspring psychopathology than chronicity.

Indeed, several indicators of severity were associated with child psychopathology in the present study. First, the lifetime prevalence of maternal suicide attempts was associated with a 3-fold increase in the lifetime prevalence of children's depressive disorders. Second, the presence of maternal comorbid disorders—another indicator of severity of maternal depression—was associated with increases in the lifetime prevalence of children's psychiatric disorders. The severity of the current depressive episode, as measured using the HAM-D_{17}, was not associated with children's outcomes. However, as previously mentioned, the range of severity of the current episode of maternal depression was narrow, a reflection of the fact that most mothers were severely depressed when they were assessed. Maternal suicidality and maternal comorbid Axis I disorders were assessed within the previous 6 months. Both most likely reflect more sustained psychopathology as opposed to current depression severity assessed in the prior 7 days.

Several findings regarding maternal comorbid psychiatric disorders are noteworthy. First, comorbid panic disorder with agoraphobia was associated with an 8-fold

increase in the offspring lifetime prevalence of depressive disorders and a 4-fold increase in the prevalence of offspring anxiety disorders, thus exceeding the impact of each of the other comorbid conditions on children's outcomes. This finding concurs with a previous report based on a study of children of depressed parents.[16] Moreover, Biederman et al.[17] reported that parental panic disorder and parental major depression, individually and comorbidly, were associated with an increased risk of separation anxiety disorder and of multiple (2 or more) anxiety disorders in offspring. They also reported a significant increase in the prevalence of major depression among children of parents with panic disorder and major depression, compared to children of parents with neither condition. Furthermore, our final model showed that maternal comorbid panic disorder was associated with both depressive and anxiety disorders in the offspring. Overall, the accumulating evidence suggests that when maternal depression is accompanied by panic disorder with agoraphobia, the deleterious impact on offspring is significantly greater than the impact of maternal depression alone.

Second, generalized anxiety disorder was selectively associated with an increased lifetime prevalence of anxiety disorders in children, but this finding fell short of conventional levels of statistical significance ($p = .06$). This finding concurs with previous reports indicating that maternal anxiety disorders are associated with offspring anxiety disorders.[50,51]

We are not aware of any prior studies of the impact of the type of maternal depression on child psychopathology. Atypical depression had the greatest impact on offspring, as reflected in a 3-fold increase in the lifetime prevalence of offspring depressive and anxiety disorders among children of mothers with atypical depression compared to all other children in the study. Why should atypical depression have a more deleterious impact on child depressive and anxiety disorders than other types of depression, even after controlling for severity of maternal depression? Even though there is controversy about the essential features of atypical depression,[52] most descriptions include significant interpersonal difficulties including chronic interpersonal rejection sensitivity (one of the DSM-IV criteria for the atypical features specifier) and histrionic personality features (not a DSM-IV criterion). Thus, significant long-standing interpersonal difficulties are associated with maternal depression characterized by atypical features. These chronic interpersonal problems may account for the greater impact on children of this type of depression.

The relationship between maternal irritable depression and child disruptive disorders suggests that they may share some genetic liability toward affect disregulation and a tendency toward anger, consistent with previous findings that depressed adults who experience anger attacks have distinct psychological and neuroendocrine profiles.[33] Alternatively, mothers with irritable depression may be more likely to engage in inadequate parenting behaviors, which increase the risk of disruptive behavior disorders in children, particularly in boys.[53,54]

Limitations

The findings reported here may not apply to children of less severely depressed mothers, such as those identified in community samples. Moreover, the focus of this study was on maternal depression. Studies that examine the relation between characteristics of paternal depression and child outcomes are needed.

We assessed only selected psychiatric disorders in the children. Even though disorders were selected based on the extensive literature on children of depressed mothers, we cannot estimate the impact of maternal depression on any of the disorders that were not assessed. Maternal comorbid conditions were assessed using the PDSQ, a screening instrument. Although the PDSQ is highly reliable,[27] it is not a diagnostic assessment. A number of mothers had multiple clinical features of depression, and therefore the types of depression assessed (atypical, anxious, melancholic, and irritable) often overlapped. Last, since these data are cross-sectional, the findings should not be seen as reflective of causal pathways.

Conclusions and Clinical Implications

A high prevalence of disruptive behavior and anxiety disorders was evident among the offspring of currently and severely depressed mothers. A history of maternal suicide attempts and of specific maternal comorbid conditions was often associated with increased risk in children. Comorbid panic with agoraphobia seems to have a particularly deleterious impact on children of depressed mothers. Atypical and irritable depression were also found to be associated with increased problems in children. Thus, clinicians need to be aware not only of the impact of maternal MDD, but also of the added impact of comorbid conditions and of specific features of maternal depression. The extent to which improvements in maternal depression predict changes in children's functioning is an important issue for future research.

Drug name: citalopram (Celexa).

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