Published in final edited form as:
J Abnorm Psychol. 2005 August ; 114(3): 409–420.

Association of Parental Depression with Psychiatric Course from Adolescence to Young Adulthood among Formerly Depressed Individuals

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Abstract

We examined whether parental major depressive disorder (MDD) is associated with course of depression and other psychopathology among formerly depressed adolescents as they enter adulthood. The sample consisted of 244 individuals (age 24) in a longitudinal study who had experienced MDD by 19. Maternal MDD was associated with MDD recurrence, chronicity, and severity, anxiety disorders, and (among sons only) lower psychosocial functioning in offspring between 19–24. Paternal MDD was associated with lower functioning. Sons of depressed fathers had elevated suicidal ideation and attempt rates in young adulthood. Recurrent paternal MDD was associated with depression recurrence in daughters but not sons. The impact of parental MDD on offspring could not be attributed to characteristics of the offspring's depression prior to 19.

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It is well-established that major depressive disorder (MDD) is a condition occurring in early adolescence, with the female preponderance emerging at that time and levels quickly reaching rates comparable to adults (e.g., Kashani et al., 1987; Lewinsohn, Hops, Roberts, Seeley, & Andrews, 1993; McGee et al., 1990). Recent studies exploring the longitudinal course of adolescent MDD (e.g., Harrington, Fudge, Rutter, Pickles, & Hill, 1990; Lewinsohn, Rohde, Klein, & Seeley, 1999; Rao et al., 1999; Reinherz, Giaconia, Hauf, Wasserman, & Silverman, 1999; Weissman et al., 1999) indicate that while most depressed adolescents recover from the index MDD episode, the risk of depression recurrence and psychiatric comorbidity in young adulthood is substantial.

Depression is increasingly being recognized as a set of heterogeneous conditions (Cicchetti & Toth, 1998; Harrington, Rutter, & Fombonne, 1986; Winokur, 1997), and it has been suggested that depressive episodes occurring in adolescence are even more heterogeneous than child or adult depression (Wickramaratne & Weissman, 1998), with a greater proportion of adolescent MDD episodes being due to developmental challenges and stressors, which are significant during this age period (Arnett, 1999). For some adolescents, the depression experience may

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This work was partially supported by National Institute of Mental Health Grants RO1 MH66023 (Dr. Klein), RO1 MH40501, RO1 MH50522, and RO1 MH52858 (Dr. Lewinsohn).

be fairly transient, whereas for others, it indicates the beginning of a more chronic and debilitating condition. Given the apparent heterogeneity of depression, longitudinal data regarding the *course* of MDD and its diversity of outcomes are essential for understanding this disorder. The primary question we address in the present study is whether parental MDD serves as a useful marker for more negative psychiatric and functioning trajectories among formerly depressed adolescents as they transition into early adulthood. The present analyses focus on participants in a longitudinal, community-based study who had experienced an episode of MDD before age 19. These formerly depressed adolescents are stratified on the basis of parental MDD (occurring before the offspring is 19 years of age) and compared on their psychiatric course between 19 and 24 years of age.

While a growing literature exists on the transmission of MDD from parents to depression *onset* in offspring (e.g., Klein, Lewinsohn, Seeley, & Rohde, 2001; Weissman et al., 1984), the factors and processes that contribute to the maintenance and course of a disorder are not necessarily the same as those that are responsible for onset (Depue & Monroe, 1986; Lewinsohn, Allen, Seeley, & Gotlib, 1999). For example, Daly, Hammen, and Rao (2000) reported that parental psychopathology predicted MDD onset but not recurrence. Similarly, genetics played a role in MDD onset but not its continuity in a recent twin study (Scourfield et al., 2003), although genetic factors have predicted the stability of depression in other twin studies (O'Connor, Neiderhiser, Reiss, Hethertington, & Plomin, 1998; Silberg et al., 1999). Steinberg and Avenevoli (2000) recently urged developmental psychopathologists to distinguish research on the determinants of onset from the determinants of course, and argued that the latter has not received sufficient attention.

Only a small number of studies have addressed the effects of parental MDD on the *course* of offspring MDD, and those that do generally address it only briefly as part of a larger focus on depression onset. Compared to depressed offspring of nondepressed parents, findings suggest that a family history of depression may be associated with greater depression severity and chronicity, MDD recurrence, psychiatric comorbidity, impaired psychosocial functioning (Lieb, Isensee, Höfler, Pfister, & Wittchen, 2002; Warner, Weissman, Fendrich, Wickramaratne, & Moreau, 1992; Weissman, Warner, Wickramaratne, Moreau, & Olfson, 1997), and suicidal behavior (Brent et al., 1993; Weissman, Fendrich, Warner, & Wickramaratne, 1992). Our first aim in the present study is to replicate and extend the previous findings regarding the impact of parental depression on the course of psychopathology in the depressed offspring.

If parental MDD is found to be associated with a negative course of offspring MDD, our second aim is to examine whether the effects of maternal or paternal MDD on young adult psychiatric and functional status of formerly depressed adolescents persist after controlling for factors that could account for, and possibly mediate, these associations. Data are available in the present study to examine potentially relevant psychiatric and demographic characteristics. Given the increased likelihood of depression in one parent given depression in the co-parent (e.g., Matthews & Reus, 2001), the first covariate was the presence of MDD in the co-parent. Second, we adjusted for demographic and psychiatric factors occurring in the offspring prior to age 19 that are found to be associated with parental MDD. If parental MDD has its strongest negative effect in association with the initial experience of MDD in adolescence, controlling for the presentation of psychopathology in adolescence might eliminate any association between parental MDD and course of disorder in the offspring. We also adjust for whether the offspring was living with the biological parent as an adolescent, which would be an important mediating factor if family environmental mechanisms account for the impact of parental depression on offspring depression course. Finally, we adjusted for the presence of current MDD in the offspring at the time of the young adult assessment, as current mood state might bias recall of the course of depression between age 19 and the T3 evaluation.

Impact of Parent and Offspring Gender

Our third aim concerns gender moderation. We believe a primary contribution of our study over previous research is a focus on the degree to which parental and offspring gender moderates the associations between parental MDD and course of offspring psychopathology. We examine the impact of maternal and paternal depression separately. The role of maternal depression on offspring depression onset has received much more research attention than paternal depression (e.g., Phares, 1992) and a recent meta-analysis (Connell & Goodman, 2002) concluded that internalizing disorders, such as depression, in offspring were more closely related to depression in mothers than to depression in fathers. Paternal depression has not been found to increase the risk of offspring depression onset beyond maternal depression in most research (Brennan, Hammen, Katz, & Le Brocque, 2002; Lieb et al., 2002; Radke-Yarrow, Nottelmann, Martinez, Fox, & Belmont, 1992, although see Marchand & Hock, 1998). On the other hand, some research suggests that differences between effects of maternal and paternal MDD on offspring are relatively minor (Dierker, Merikangas, & Szatmari, 1995; Jacob & Johnson, 1997; Phares, Duhig, & Watkins, 2002), and a recent meta-analysis (Kane & Garber, 2004) concluded that father's depression had a significant but modest effect on offspring internalizing symptoms and disorder. The available research on the effects of depressed parent's gender on offspring depression concerns onset; the present study is the first study to our knowledge that explicitly examines effects of maternal and paternal MDD on course of offspring depression. Given the general pattern of findings and the fact that no research suggests that paternal depression is more debilitating than maternal depression, we predict that maternal MDD will be more strongly associated with the course of psychopathology in formerly depressed adolescents than paternal MDD.

Our analyses also examine the possibility of different outcomes as a function of offspring gender. Goodman and Gotlib (1999) suggest that daughters are at greater risk than sons for experiencing maladaptive effects of parental depression. The heritability of MDD in twin studies has varied by gender of the offspring, being higher for female offspring in some research (Kendler, Gardner, Neale, & Prescott, 2001; Scourfield et al., 2003) but not others (Eley & Stevenson, 1999). Female gender may have a stronger association with depression incidence than with depression recurrence. Several studies have noted that women have higher rates of first onset but not greater persistence or recurrence (Hankin et al., 1998; Kessler, 2003; Kovacs, 2001; Lewinsohn, Rohde, Seeley, Klein, & Gotlib, 2000; Wainwright & Surtees, 2002), although adult female patients have been found to have higher rates of recurrence compared to adult male patients (Kuehner, 1999; Mueller et al., 1999), which may be related to differences in ruminative cognitive style (Kuehner & Weber, 1999). In the present study, we examine whether factors associated with parental MDD predispose formerly depressed daughters to a more negative course compared to formerly depressed sons.

The course of offspring depression may also be influenced by interactions between parent gender and offspring gender. Specifically, girls may be at particular risk for depression as a function of maternal depression. Girls spend a greater proportion of their time with their parents than boys (Montemayor, 1983), and mothers tend to report more conflict with daughters than with sons (Hill, Holmbeck, Marlow, Green, & Lynch, 1985). Maternal depression symptoms have been found to be associated with depression symptoms in girls but not boys (Davies & Windle, 1997; Fergusson, Horwood, & Lynskey, 1995; Thomas & Forehand, 1991). Sheeber, Davis, and Hops (2002) proposed a model of same-gender transmission in which the family normalizes depressive behaviors in women and fails to reinforce instrumental behaviors in daughters. Modeling hypotheses also predict that there should be an interaction between the gender of the depressed parent and the gender of the child, with greater risk in same-gender pairs (Connell & Goodman, 2002). Unfortunately, few studies have explored this issue with respect to depression onset, and, to our knowledge, no research has examined the impact of

parent and offspring gender on relations between parental depression and the course of offspring depression. Our general hypothesis is that same-gender effects will be stronger than cross-gender effects.

Characteristics of Parental MDD

Our fourth aim is to examine the degree to which aspects of the parental MDD moderate the effects of parental depression on the course of disorder in formerly depressed offspring. Previous research suggests that early onset or recurrent MDD episodes in parents are among the strongest predictors of MDD *onset* in offspring (Beardslee et al., 1996; Keller et al., 1986; Kupfer, Frank, Carpenter, & Neiswanger, 1989; Orvaschel, 1990; Orvaschel, Walsh-Allis, & Ye, 1988; Warner, Mufson, & Weissman, 1995; Weissman, Leckman, Merikangas, Gammon, & Prusoff, 1984; Weissman, Warner, Wickramaratne, & Prusoff, 1988). Early onset of parental MDD is generally assumed to confer more genetic liability (Todd et al., 1993) but early MDD onset in the parent would also be generally associated with greater exposure to the depressed parent and exposure at an earlier developmental period for the offspring. Similarly, recurrent MDD in the parent would generally be associated with greater exposure to depression in the offspring. In the present study, we examine whether early onset or recurrent MDD in the parent is associated with a more negative *course* of psychopathology and functioning in formerly depressed offspring.

The present study extends our previous research, which has documented the high degree of MDD continuity from adolescence into young adulthood (Lewinsohn et al., 1999), the aggregation of MDD within families (Klein et al., 2001), and the fact that familial loading of recurrent MDD predicts depression recurrence in formerly depressed adolescents (Lewinsohn et al., 2000). The present study is most closely related to a recent study in which we examined the impact of parental gender and clinical characteristics of parental MDD on the incidence of MDD and other psychopathology in adolescent and young adult offspring of depressed parents (Klein, Lewinsohn, Rohde, Seeley, & Olino, in press). In that paper, we reported that maternal MDD was significantly associated with the incidence of MDD in offspring. In contrast, paternal MDD was only associated with the onset of MDD among offspring with moderate-severe episodes. There was considerable diagnostic specificity in that parental non-mood disorders did not predict rates of MDD in offspring and parental MDD did not predict rates of non-mood disorders in offspring. Finally, rates of MDD were particularly elevated in offspring of parents with early-onset MDD. The current study extends our previous research by addressing very specific questions regarding the psychiatric trajectories taken by formerly depressed adolescents as a function of gender and various aspects of parental depression.

Method

Participants and Procedures

Offspring—A concerted effort was made to assemble a representative sample of community-residing adolescents for the initial (T1) sample. The population for this sample was the total enrollment (approximately 10,200) of nine high schools in two urban and three rural communities in western Oregon. Sampling within each school was proportional to size of school, size of grade within school, and gender within grade. T1 diagnostic interviews and questionnaire assessments were conducted between 1987–1989 with 1,709 adolescents (14–18 years of age, 61% participation rate). Approximately one year later (T2), 1,507 (88%) of the T1 participants returned for a re- administration of the interview and questionnaire (mean T1–T2 interval = 13.8 months, *SD* = 2.3). Checks regarding the representativeness of the T1 sample and the impact of attrition from T1 to T2 have been previously described (Lewinsohn et al., 1993) and indicate that the study participants may be considered representative of high school students in western Oregon. Most importantly, there were no indications that

participants differed from non-participants or individuals who discontinued participation on diagnostic or dimensional measures of depression.

Between 1994–1999, a third (T3) wave of questionnaire and diagnostic interviews was conducted with selected participants after they had turned 24 years of age. We attempted to interview participants with a T2 lifetime history of MDD (n = 360), participants with a T2 history of nonaffective disorder (n = 284), and a randomly-selected subset of participants with no history of mental disorder at T2 (n = 457 of 863; all non-White T2 participants with no history of disorder at T2 were retained in the sample to enhance the ethnic representation of the T3 group). Of the 1,101 participants selected for T3, 941 (85%) completed the mailer questionnaire and the T3 diagnostic interview, which was conducted by telephone (see Rohde, Lewinsohn, & Seeley, 1997 for data on the comparability of telephone and face-to-face assessment formats). The mean time between the T2 and T3 assessments was 6.8 years (SD = 1.4). Although women were more likely than men to complete the T3 assessments (89% vs. 81%);$\chi^2(1, N = 1101) = 13.55$, $p < .001$, T3 participation differences as a function of other demographic variables or T2 diagnostic status, including a history of MDD at T2, were nonsignificant.

Written informed consent was obtained from participants (and their guardians, if applicable) to conduct all assessments.

Parents—As a separate project, biological parents and full siblings of the T3 participants were recruited and interviewed for lifetime psychopathology, with the goal of obtaining two sources of data for each family member (either direct and informant interviews or two informant interviews). Psychiatric data were obtained between 1995 and 1998 on 802 families (85% of T3 interviewed participants), which represented 2,646 individuals (804 mothers, 787 fathers, and 1,055 siblings). Only data on parental psychopathology were used in the present study.

The sample for the present study was restricted to T3 participants who had experienced and recovered from an episode of MDD prior to 19 years of age and on whom we had data on parental psychopathology (n = 244). Among mothers of the 244 participants, 178 (73%) participated in the direct interviews. Two sources of maternal diagnostic data were available for 203 (83%) of the families, most commonly a direct interview with the mother and an informant interview with the OADP participant (n = 165). One source of diagnostic data for mothers in the remaining 41 (17%) families was available, usually an informant interview with the OADP participant (n = 36). Fewer fathers provided direct interviews (n = 95, 39%). However, two sources of diagnostic data were obtained for 195 (80%) of the fathers, most often (a) a direct interview with the father plus an informant interview with the OADP participant (n = 81), or (b) two informant interviews with the mother (spouse of father) and the OADP participant (n = 74). One source of diagnostic data for father in the remaining 49 (20%) families was available, most often an informant interview with the OADP participant (n = 35).

Diagnostic Interviews

Offspring—Participants were interviewed at T1 with a version of the Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS, Orvaschel, Puig-Antich, Chambers, Tabrizi, & Johnson, 1982) that combined features of the Epidemiologic version and the Present Episode version, and included additional items to derive DSM-III-R (American Psychiatric Association, 1987) diagnoses. At T2 and T3, participants were interviewed using the Longitudinal Interval Follow- up Evaluation (LIFE, Keller et al., 1987), which elicited detailed information about the course of psychiatric disorders since the previous interview, adapted for DSM-IV (American Psychiatric Association, 1994) criteria.

Most interviewers had an advanced degree in psychology or social work, and all were extensively trained prior to data collection. Based on a randomly selected subsample at T1 and T2 (n = 233), interrater reliability for lifetime diagnoses were good to excellent: MDD k = .86, kappas for non-mood disorder categories ranged from k = .76 to .89. For the T2–T3 period (n = 178), interrater reliability was excellent: MDD k = .87, non-mood disorder k = .82.

Parents—Parents were directly interviewed using the Structured Clinical Interview for DSM-IV, nonpatient version (SCID-NP; Spitzer, Williams, Gibbon, & First, 1992). Family history informant data were collected using a revised version of the Family Informant Schedule and Criteria (FISC; Mannuzza & Fyer, 1990) modified for DSM-IV criteria. Kappas for the interrater reliability of lifetime diagnoses were excellent, all kappas from both SCID-NP (n = 157) and FISC (n = 242) interviews were greater than .80, with the exception of anxiety disorders as per FISC (k = .77).

We examined the sensitivity and specificity of informants' reports by comparing FISC diagnoses to SCID diagnoses for parents who had both sources of data available. Sensitivity varied according to the informant and target, but specificity was consistently acceptable. With the OADP proband (offspring) as the informant, sensitivity and specificity for MDD in mothers (n = 523) was .45 and .85, respectively; sensitivity and specificity for MDD in fathers (n = 316) was .32 and .90, respectively. With another family member (generally the co-parent) as the informant, sensitivity and specificity for MDD in mothers (n = 59) was .30 and .80, respectively; sensitivity and specificity for MDD in fathers (n = 40) was .66 and .82, respectively. The high sensitivity of other family members' reports of paternal MDD likely reflects the fact that the other family member informant was generally the mother, and mothers tend to have the best knowledge of family members (Cohen, 1988). Finally, the correlations between informants' reports of the age of onset of MDD on the FISC and parents' reports of age of onset of MDD on the SCID for cases in which both the parent and informant agreed on the presence of MDD were .43 for mothers (n = 77, $p < .001$) and .47 for fathers (n = 26, $p < .05$).

As data were available from multiple informants for most parents, we derived lifetime DSM-IV diagnoses for the parents using the "best-estimate" procedure (Leckman, Sholomskas, Thompson, Belanger, & Weissman, 1982). Two diagnosticians, from a team of four senior clinicians, independently reviewed all information from the SCIDs and FISCs without knowledge of offspring diagnoses, and made best-estimate diagnoses for the parents using the guidelines in Klein, Ouimette, Kelly, Ferro, and Riso (1994). The diagnosticians' conclusions were then compared, and disagreements were resolved by consensus. Interrater reliability of the independently derived best-estimate diagnoses prior to the resolution of discrepancies exceeded k = .90, indicating excellent agreement.

Outcome Variables: Course of MDD and Functioning from 19 to 24

Depression characteristics consisted of (a) MDD recurrence between 19–24 (Yes/No), (b) MDD chronicity, which was defined as the number of weeks the participant was in an episode of MDD between ages 19–24 (*ICC* = .99), (c) MDD severity, which was defined as the maximum number of MDD symptoms experienced during the time period (range = 0–9; *ICC* = .90), and (d) the development of mania (i.e., switching from unipolar to bipolar disorder; k = 0.74 for this low baserate occurrence).

Suicidal behavior consisted of (a) the presence of suicidal ideation, which was defined as the number K-SADS symptoms (i.e., thoughts of death, wishing to be dead, suicidal ideation, suicidal plan) experienced during the worst MDD episode between 19–24 (*ICC* = 0.83), and (b) a suicide attempt occurring between the ages of 19–24 (Yes/No) (k = 0.90).

Psychiatric comorbidity consisted of two diagnostic categories common in young adulthood: (a) anxiety disorders (i.e., panic disorder with or without agoraphobia, specific phobia, social phobia, obsessive-compulsive disorder, post-traumatic stress disorder, acute stress disorders, generalized anxiety disorder) ($k = 0.87$), and (b) substance use disorders (i.e., abuse or dependence) ($k = 0.81$).

Low psychosocial functioning was defined as a DSM-IV Global Assessment of Functioning (GAF) score at the time of the T3 assessment (*ICC* unavailable).

Statistical Analyses

We first examined the associations of young adult outcomes as a function of either maternal or paternal MDD using logistic regression to predict the dichotomous outcome measures, and linear regression to predict the continuous outcome measures. To ensure that the direction of temporal effects was unambiguous, the parent's first episode of MDD had to occur prior to the offspring turning 19. In addition, analyses controlled for whether the parental diagnostic data had been obtained directly from the parent (yes/no). This first set of analyses also examined whether offspring gender or the source of parental diagnostic data (direct report; yes/no) moderated any of the associations.

Next, associations were adjusted for the following potential confounding or mediating factors, in addition to source of parental diagnostic data: (a) MDD in the co-parent, (b) characteristics of the offspring's MDD or other psychiatric factors prior to age 19 that were found to be associated with parental MDD, (c) whether the offspring was living with the parent at T1, and (d) the presence of current MDD at the T3 assessment (4% of the sample), which may have biased recall of previous psychiatric functioning.

The last set of analyses examined the degree to which early onset or recurrent MDD in the parent (as opposed to late onset or single episodes of MDD) were associated with more negative psychiatric outcomes among formerly depressed offspring. Analyses were computed separately for maternal and paternal MDD and were restricted to the subset of offspring with parental depression. MDD onset age in the parent was treated as a continuous measure. Analyses examined the impact of main effects and two-way interactions with offspring gender and source of parental diagnostic data. For analyses involving the entire sample, power greater than .80 was available to detect small-medium effects. For the analyses on parental MDD characteristics (onset age and recurrence), adequate power was available to detect medium to large effects in association with characteristics of maternal MDD and large effects only in association with paternal MDD. Given our interest in balancing concerns with Type I versus II errors, alpha was set at $p < .05$ throughout the analyses.

Results

Descriptive Characteristics of the Sample

Of the 244 formerly depressed adolescents in the present study, 101 (41%) had a mother with a history of MDD and 74 (30%) had a father with a history of MDD occurring prior to the offspring's 19th birthday. We first examined whether maternal or paternal MDD was associated with T2 demographic characteristics or psychiatric characteristics of the offspring prior to the age 19. Demographic differences between offspring as a function of parental MDD were nonsignificant. The mean age of sample at T2 was 17.9 (*SD* = 1.2) years; 70% were female, 91% were White, and 38% had one or more parents with a Bachelors degree. Approximately one-third (35%) were living with both biological parents at T2; an additional 33% lived with their biological mother but not father, and 6% lived with their biological father but not mother. The remaining 26% ($n = 63$), who were no longer living with either biological parent, had a

mean age of 18.8 years (*SD* = 1.0) and were attending college (*n* = 23), living with other relatives (*n* = 9), or living on their own (*n* = 31).

The presence of either maternal or paternal MDD was not associated with the number of MDD episodes occurring before age 19 (*M* = 1.3, *SD* = 0.6), onset age (years) of first MDD episode (*M* = 15.0, *SD* = 2.7), number of weeks in MDD episodes prior to age 19 (*M* = 22.5; *SD* = 52.2), or a history of dysthymia by age 19 (7%). Differences as a function of parental depression were, however, significant for the two remaining variables: (a) presence of non-mood disorders prior to age 19 (59% given maternal MDD vs. 45% given no maternal MDD; $\chi^2(1, N = 244) = 5.08$, $p = .024$; 61% given paternal MDD vs. 45% given no paternal MDD; $\chi^2(1, N = 244) = 4.24$, $p = .039$), and (b) presence of non-mood disorders in the parents prior to the offspring turning 19 (73% given maternal MDD vs. 61% given no maternal MDD; $\chi^2(1, N = 244) = 4.07$, $p = .044$; 78% given paternal MDD vs. 61% given no paternal MDD; $\chi^2(1, N = 244) = 7.27$, $p = .007$). Of the mothers with MDD, lifetime rates of anxiety and substance use disorders were 28% and 36%, respectively (compared to 11% and 20%, respectively, for mothers with no history of MDD). Of the fathers with MDD, lifetime rates of anxiety and substance use disorders, were 19% and 65% (compared to 6% and 45%, respectively, for fathers with no MDD history).

Association of Parental MDD with Course of Psychopathology and Functioning in Offspring

Formerly depressed offspring were compared on characteristics of depression, suicidality, psychiatric comorbidity, and psychosocial functioning between 19–24 as a function of maternal and paternal MDD. Rates of the various outcomes as a function of parent and offspring gender are shown in Table 1. The first set of analyses, which were adjusted for the source of parental diagnostic data, are shown as Model 1 in Table 2. Five of the 10 examined variables had a significant main effect association with maternal depression. Specifically, formerly depressed offspring with depressed mothers were more likely to experience MDD recurrence and comorbid anxiety disorders, have greater depression chronicity and severity, and lower psychosocial functioning at T3 compared to formerly depressed offspring of nondepressed mothers. The presence of paternal MDD had a main effect association with one outcome: lower psychosocial functioning at age 24.

Interactions with offspring gender—Offspring gender moderated the impact of parental MDD on three young adult outcomes. Maternal MDD interacted with offspring gender in relation to offspring psychosocial functioning at age 24, *semi-partial correlation (sr)* = −.13, $p = .045$. Paternal MDD interacted with offspring gender in relation to suicidal ideation, *sr* = .13, $p = .048$, and suicide attempt in the offspring, *OR* = 2.15 (95% *CI* = 1.08–4.26), $p = .029$. Examining the outcomes separately by gender suggested that parental MDD was associated with problematic functioning in these outcome areas for the sons of depressed parents but not the daughters. Mean GAF scores were significantly lower for male offspring with depressed mothers (*M* = 72.5, *SD* = 12.5) relative to other formerly depressed males (*M* = 79.5, *SD* = 6.9); $t(70) = -3.05$, $p = .003$. Comparable differences for female offspring were nonsignificant, *M* = 76.3 (*SD* = 9.3) vs. *M* = 77.4 (*SD* = 9.3); $t(170) = -0.74$, $p = .461$. Suicidal ideation levels were (nonsignificantly) higher for male offspring with depressed fathers (*M* = 0.81, *SD* = 1.3) relative to male offspring of nondepressed fathers (*M* = 0.33, *SD* = 0.84); $t(70) = 1.91$, $p = .060$. Differences for female offspring as a function of paternal MDD were nonsignificant, *M* = 0.42 (*SD* = 0.87) vs. *M* = 0.43 (*SD* = 0.92); $t(170) = -0.07$, $p = .945$. Rates of suicide attempt were 23% among male offspring with depressed fathers compared to 2% among male offspring with nondepressed fathers; $\chi^2(1, N = 72) = 8.27$, $p = .004$. Differences among female offspring in the two groups were nonsignificant, 4% vs. 6%; $\chi^2(1, N = 171) = 0.16$, $p = .688$.

Interactions with source of parental diagnostic data—Whether the parent had been directly interviewed moderated the impact of parental MDD on one young adult outcome. Maternal MDD interacted with source of parental diagnostic data in relation to suicidal ideation in the offspring during the 19–24 age period, *sr* = −.16, *p* = .014. Examining the outcomes separately by direct versus informant only data suggested that maternal MDD was associated with suicidal ideation in the offspring only when mothers were not directly interviewed. For the 178 participants who mothers had been directly interviewed, the association between maternal MDD and offspring suicidal ideation in young adulthood was nonsignificant; *sr* = −0.07; *p* = .350. For 95 participants whose mothers had not participated, maternal MDD was associated with offspring suicidal ideation, *sr* = .31, *p* = .010; mean (*SD*) suicidal ideation in the offspring with maternal MDD was 0.84 (1.21) versus 0.27 (0.74) in offspring of nondepressed mothers.

Adjusting for Potential Confounding or Mediating Factors in the Associations with Parental MDD

To examine the possibility that other factors accounted for or mediated the significant associations with parental MDD, outcome variables in the offspring that had a significant association with maternal or paternal MDD were re-analyzed controlling for (a) MDD in the co-parent, (b) the two adolescent offspring characteristics that were associated with parental MDD (i.e., presence of non-mood disorder in the offspring by age 19, presence of parental non-mood disorder prior to the offspring turning 19 years of age), (c) whether the offspring had been living with the parent at T1, and (d) whether the offspring was in a current episode of MDD at T3. Results are shown as Model 2 in Table 2.

Adjusting for these five covariates (in addition to source of parental diagnostic data) reduced two of the five previously-significant main effect associations with maternal MDD to nonsignificance: MDD severity and GAF scores at age 24. Psychosocial functioning at age 24, however, had been significant only for male offspring and that association remained significant after the adjustments, *sr* = .28, *p* = .021. The three other outcomes remained significantly associated with maternal MDD in this rigorously controlled analysis.

Adjusting for the covariates reduced the main effect association of paternal MDD with T3 GAF score to nonsignificance. Adjusting for covariates in the gender-moderated findings, higher rate of suicide attempts among male offspring with depressed fathers remained significant, *OR* = 7.40 (95% *CI* = 1.50–36.35), *p* = .014, although the presence of suicidal ideation in male offspring was no longer significantly associated with paternal MDD, *sr* = .24, *p* = .053.

Examination of the potential confounding or mediating factors for the outcomes that became statistically nonsignificant in Model 2 indicated that only one factor -- current MDD at age 24 (T3) -- had a significant effect. None of the other potential mediating factors had a significant association with the young adult outcomes.

Association of Parental MDD as a Function of Parental MDD Onset Age and Recurrence

The last set of analyses examined whether early onset or recurrence of MDD in the parent predicted any of the psychiatric or functional outcomes in the offspring during the 19–24 age period. Results were conducted separately for offspring with maternal and paternal depression and were restricted to the subset of offspring with parents with MDD. Results were adjusted for source of parental diagnostic data and interactions with offspring gender and source of parental diagnostic data were considered. Neither MDD onset age or the presence of recurrent MDD episodes in either the mother or the father had a main effect association with any of the offspring outcomes. However, three interactions were significant and are described next.

Interactions with offspring gender—Offspring gender moderated the association between recurrent paternal MDD and recurrence in the offspring, *OR* = 1.79 (95% *CI* = 1.06–3.04), *p* = .030. Recurrent paternal MDD was associated with recurrence in daughters; 62% of daughters with recurrent paternal MDD experienced recurrence themselves vs. 27% of daughters whose father had a single MDD episode; $\chi^2(1, N = 48) = 5.64$, $p = .018$. The association for sons was nonsignificant; 36% vs. 53%, respectively; $\chi^2(1, N = 26) = 0.73$, $p = .391$.

Interactions with source of parental diagnostic data—The source of parental diagnostic data moderated two associations between onset age of parental MDD and offspring outcomes: onset of maternal MDD in predicting MDD chronicity in the offspring, *sr* = .24, *p* = .016; and onset of paternal MDD in predicting anxiety disorders in the offspring, *OR* = 1.01 (95% *CI* = 1.00–1.02), *p* = .009. An earlier onset of maternal MDD was significantly associated with MDD chronicity in offspring given direct maternal report (*sr* = .251, *p* = .029) but not when only informant reports were available (*sr* = .18, *p* = .379). The interaction for onset of paternal MDD with anxiety disorder in the offspring was in a counter-intuitive direction. For direct report of paternal MDD onset age, the association with anxiety disorders in the offspring was nonsignificant (*OR* = 0.99, *95% CI* = 0.98–1.01; *p* = .247). When direct report from the father was not available, informant report of later paternal MDD onset was associated with anxiety disorders in the offspring (*OR* = 1.02, *95% CI* = 1.00–1.03; *p* = .027). It should be noted that the number of offspring with anxiety disorders in these two groups were extremely low (4 and 6 cases, respectively).

Because paternal MDD had been found to be associated with suicidal ideation and attempt in male offspring, we also divided the depressed fathers into those with or without suicidal behavior to examine whether rates of suicidality in the male offspring would be higher given paternal suicidality. Rates of both suicidal ideation and suicide attempt in male offspring did not differ as a function of paternal suicidality, $t(18) = 1.98$, $p = .063$ and $\chi^2(1, N = 20) = 0.01$, $p = .999$, respectively.

Discussion

Our goal in this study was to examine whether the history of MDD in a biological parent serves as a useful marker for divergent psychiatric and functioning pathways among formerly depressed adolescents as they transition into early adulthood. While the literature on familial transmission of depression is growing, it has focused primarily on the relation between parental MDD and depression incidence in the offspring. In the present study, all of the offspring had already experienced an episode of MDD by adolescence. Our interest was in whether maternal or paternal depression had detectable associations with the psychiatric course of the formerly depressed adolescent as he or she becomes a young adult, given that they are entering this important developmental period with a history of depression. We were particularly interested in whether gender, of either the parent or offspring, moderated any of these associations. It is increasingly being recognized that the variables related to the maintenance and course of depression may differ from those related to first incidence. Other contributions of the present study are that participants were selected from the community rather than patient samples, and that attempts were made to directly interview parents wherever possible. Much of the previous research on parental MDD has relied on patient samples, which may not be representative of the broader population of depressed individuals. In their recent meta-analysis of the effects of paternal depression on offspring internalizing problems, Kane and Garber (2004) found that effects were greatest when community samples were examined, presumably because of restricted variance in patient samples. In addition, the adult offspring are often interviewed regarding the presence of psychopathology in their parent, which may be somewhat insensitive, whereas we attempted to interview parents directly whenever possible.

Consistent with the conclusions drawn by Connell and Goodman (2002) in their meta-analysis examining associations between parental and offspring psychopathology, maternal depression in the present study had more negative associations with offspring course compared to paternal MDD. Specifically, in the initial main effects models, depression in the mothers was related to greater MDD recurrence, chronicity, and severity; higher rates of anxiety disorders; and lower psychosocial functioning in the offspring. Conversely, depression in the fathers was associated with only one outcome measure: lower psychosocial (GAF) functioning in young adulthood. Our findings are consistent with others who have found that a family history of depression is a marker for a poorer course among depressed children and adults (Akiskal, 1982; Beardslee, Keller, Lavori, Staley, & Sacks, 1993; Kendler, Walters, & Kessler, 1997; Weissman et al., 1997).

Three associations were moderated by gender of the offspring. In each, parental depression was associated with poorer outcomes for formerly depressed sons but not daughters. Specifically, the association of maternal depression with lower psychosocial (GAF) functioning was limited to male offspring, and both measures of suicidality in offspring (i.e., suicidal ideation and suicide attempt) were elevated in the sons of depressed fathers relative to the sons of nondepressed fathers (and all daughters). The fact that offspring gender-specific interactions involved the sons of depressed parents but not daughters was counter-intuitive given previous research. This unexpected pattern of results may have to do with the fact that all of the offspring in this study had already experienced an episode of MDD; perhaps boys who reach this threshold are particularly susceptible biologically or psychologically to the effects of parental depression. In addition, two of the three gender-specific associations pertained to sons and fathers, which would be consistent with the same-gender effects model. Second, these two son-father specific interactions involved measures of suicidality, which is associated with other psychiatric factors in addition to depression (e.g., Brent & Moritz, 1996). The effects of a father's depression on suicidality in the son were quite striking, with more than a sevenfold increase in suicide attempts given paternal MDD. Almost one quarter of the sons of depressed fathers attempted suicide between the ages of 19–24. Rates of suicide attempts in the other groups of formerly depressed offspring were only 2–6%. If replicated, this association could indicate a significant same-gender marker in the identification of young men most at risk for future suicidal behaviors.

The association of maternal depression with psychiatric comorbidity in the young adult offspring was restricted to internalizing disorders: 14% of the formerly depressed adolescents with depressed mothers had experienced anxiety disorders in young adulthood, compared to only 5% of the formerly depressed adolescents with no maternal MDD history. This is consistent with evidence of intergenerational transmission of some anxiety disorders in the offspring of depressed parents (Silberg & Rutter, 2002; Weissman, Warner, Wickramaratne, Moreau, & Olfson, 2000). The presence of depression in either parent did not increase the likelihood of switching from MDD to bipolar disorder or the development of other psychiatric comorbidities, although it was noteworthy that almost all of the results were in the direction of greater psychopathology given depression in either parent.

The impact of parental MDD on course of disorder in the formerly depressed offspring was not due to characteristics of the offspring's depression prior to age 19. Formerly depressed adolescents with parental depression did not differ from formerly depressed adolescents with no history of parental depression on adolescent demographic factors or on the aspects of adolescent mood disorder that we examined (i.e., onset age of MDD, number or duration of MDD episodes, presence of dysthymia prior to 19 years of age). It is possible that the absence of associations between parental MDD and aspects of adolescent depression in the offspring may have been due to limited variance in the presentation of psychopathology in our sample

prior to age 19. Having a depressed parent was, however, associated, with a greater likelihood of non-mood disorders in both the depressed adolescent and parent.

Controlling for the various potential confounding or mediating factors did not appreciably reduce the magnitude of the associations, although it should be noted that we examined only a very limited number of factors. These adjustments reduced two of the five previously-significant main effect associations with maternal MDD to the level of a statistical trend; the other three main effect associations with maternal MDD and the one main effect association with paternal MDD remained significant. When we examined which of the additional factors weakened the association with parental MDD, only one measure – the presence of a current episode of MDD at age 24 -- had a significant association with any of the young adult outcomes and its strongest influence was on the outcome measure of psychosocial functioning (GAF) at age 24. This association is almost guaranteed by the fact that both measures referred to the offspring's current state at the time of the third assessment. We believe these controls provided a very rigorous test of the associations of parental depression with course of psychopathology in formerly depressed offspring, strengthening the conclusion that maternal depression is associated with a noticeably poorer course of depression in offspring.

In addition to adjusting for the source of parental diagnostic data (direct versus informant), we also considered the possibility that the presence of a direct parent report might moderate the associations. Informants, especially offspring, may not have much knowledge of depression in their parents, especially detailed information regarding earlier onset and recurrent depressive episodes occurring when the offspring was just a child. Regarding the impact of data source on the main effect analyses, only one interaction was present: maternal MDD as assessed by informant report predicted suicidal ideation in the offspring but not when mothers were directly interviewed. The finding needs to be replicated but one possible explanation is that suicidal ideation in the offspring may be associated with greater psychopathology (or suicidality, specifically) in the mothers, which was related to their nonparticipation in the project. Alternatively, mother non-participation could be a marker for greater family dysfunction, which might increase suicidality in offspring with a familial vulnerability for depression.

Restricting our analyses to biological parents with presumably more serious forms of depression had a fairly subtle impact. Among the parents with depression, outcomes in the offspring were not associated with main effects of earlier onset or recurrence in the parent. However, one interaction with offspring gender emerged: recurrent depression in the fathers before the offspring was 19 predicted recurrent MDD in daughters in young adulthood. In a previous study examining a large set of psychosocial and familial predictors of MDD recurrence during this same time period (Lewinsohn et al., 2000), we found that a higher proportion of family members (parents and siblings) with recurrent MDD was a strong predictor of recurrence in the offspring. The present findings, which were restricted to parents and required that the parent's depression began before the offspring outcome, suggest the more specific nature of that association.

The source of parent diagnostic data moderated two outcomes in the analyses examining onset age or recurrence of parental MDD. We assumed that direct parent report would be particularly important in these fine-grained analyses, due to the modest correspondence between informants' and parents' reports of clinical characteristics of MDD in the parents. In the first interaction, earlier onset of maternal depression was associated with chronicity in offspring when mothers provided direct report but not based on informant information. In the second interaction, a later onset of paternal depression by informant report was associated with significantly higher rates of anxiety disorders in the children; this association was not found when fathers reported directly on their depressive history. This second interaction was based

on only ten cases of anxiety disorder in the offspring and is considered suspect pending replication.

If our findings that parental MDD influence the course of MDD in offspring are replicated, these associations could be due to genetics or several environmental processes. Several theories related to the maintenance and course of depression focus on environmental factors that could be related to parental depression, including childhood adversity (Gilman, Kawachi, Fitzmaurice, & Buka, 2003; Brown & Moran, 1994), harsh parental discipline (Lara, Klein, & Kasch, 2000), parent divorce (Warner et al., 1992), and expressed emotion (e.g., McCleary & Sanford, 2002). In addition, genetic factors could influence the presentation of depression through main effects, effects mediated by emotional disturbance, or changes that predispose the person to stress sensitivity (Kendler, Gardner, & Prescott, 2002; Rutter, 2003). Family data such as the present study cannot distinguish genetic from environmental factors; twin or adoption studies are needed for that. It is misleading, however, to assume an easy separation of genetic versus environmental variance (Rutter, 2003) and, consistent with a multifactorial model of psychopathology, gene-environment interactions are increasingly being recognized (Cadoret, Yates, Troughton, Woodworth, & Stewart, 1995; Caspi et al., 2002). We believe that the first step in this process is to document the impact of parental MDD on the trajectories of depression in offspring. Future research, probably involving a much more detailed assessment of the parent, child, and home environment, are needed to address the mechanisms accounting for these associations.

The study has several potential limitations. First, not all relatives were directly interviewed. Therefore, we had to rely on informant reports in some cases, which resulted in lowered sensitivity, especially regarding depression in fathers. In addition, more mothers provided direct diagnostic reports than fathers. Therefore, we adjusted for the source of parental diagnostic data in all analyses and examined whether source of parental data moderated an association.

Second, data for the parents were based on lifetime retrospective ratings and data for the offspring at the T3 covered an average period of seven years. This may have resulted in biased recall, especially for the small number of participants who were in a current MDD at the time of the T3 interview. We attempted to address this confound by controlling for current MDD state at T3 in the adjusted analyses. It should be noted, however, that this approach may have "overcontrolled" for the impact of current MDD. If parental MDD is truly associated with higher recurrence rates and greater chronicity among offspring, it will by definition also be associated with a greater likelihood that the offspring will be depressed at any point in time (i.e., the current MDD is a *consequence* of greater recurrence and chronicity rather than an *artifactual cause*).

Third, our sample consisted of individuals who had developed depression prior to age 19. It is possible that the relations between parental depression and course of offspring MDD may differ for individuals with prepubertal versus postpubertal MDD onset (Harrington et al., 1997). We merged those two potentially distinct subgroups of offspring due to the small number of participants with prepubertal MDD.

Fourth, our focus was restricted to biological parents. While this allowed us to examine specific factors related to gender and MDD characteristics within the parent, depression within the siblings and grandparents may have important effects (Kovacs, Devlin, Pollock, Richards, & Mukerji, 1997; Orvaschel, 1990; Warner, Weissman, Mufson, & Wickramaratne, 1999). In addition, if environmental mechanisms predominantly account for the impact of parental depression on the course of depression in offspring, the inclusion of step-parents in a study would be critical. There is currently stronger evidence for genetic than shared familial

environmental effects on depression (Sullivan, Neale, & Kendler, 2000) and this fact informed our original design decision to restrict our assessments to biological parents. The fact that we cannot comment on the impact of depression in step-parents on course of offspring psychopathology is a limitation of the present report.

Fifth, the sample was restricted to OADP participants whose parents had also participated in the companion study. In addition to the 244 formerly depressed participants who formed the subject pool for the present study, an additional 45 OADP participants had a history of MDD prior to age 19 but their parents had not provided diagnostic data. We compared the 244 participants from the present study to the 45 participants excluded from the present study on the examined young adult outcome measures; all differences were nonsignificant, which suggests that the present findings were not biased by differential rates of parental participation in our project.

Sixth, several of the offspring course characteristics examined in the present study were probably correlated. In addition, our measures of the characteristics of the offspring's depression may have been somewhat insensitive (e.g., other methods for evaluating the severity of depression or psychosocial functioning could have been examined) and caution is needed in interpreting the negative, as well as positive, findings.

Lastly, a large number of comparisons were computed, which increased the potential for experiment-wide error. We did not statistically adjust for experiment-wide error, opting instead to rigorously control for several potential confounding or mediating factors. Our decision to not control for Type I error was made to balance this issue with avoiding a Type II error, given the statistical power for the analyses. We were adequately powered to detect small to medium effects in analyses using the entire sample but could detect only medium to large effects in association with MDD onset age or recurrence in the parents. Future research is needed to replicate the present results and evaluate whether the course of formerly depressed adolescents of depressed and non-depressed parents will continue to diverge or will begin to converge as the formerly depressed offspring move further into adulthood.

Clinical implications of the present study include the need for particularly intensive treatment and monitoring of depressed adolescents and young adults who have a depressed parent, especially the mother. This subgroup of depressed adolescents may benefit from maintenance therapy. A history of maternal depression also increases the likelihood of comorbid anxiety disorders in the depressed adolescent or young adult, which might warrant separate treatment. Our findings suggest that parental depression has an equally negative effect on the course of depression in formerly depressed sons and daughters but may more negatively influence the psychosocial functioning and potential for suicidality of sons, which warrants particularly close monitoring of risk. The presence of parental depression appears to be a salient selection criteria for identifying formerly depressed adolescents in need of prevention treatments aimed at reducing the development of recurrent, chronic, or severe depression in young adulthood. The present study also suggests that depressed clients who are parenting may require additional support. Although we do not know what mechanisms mediate the association between parental depression and the trajectory of depression in offspring, clinicians treating depressed parents need to evaluate potential contributing factors (e.g., parenting skills, expressed emotion, modeling of depressotypic coping patterns) and address those that can be modified.

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Table 1

Rates of Psychiatric Outcomes in Formerly Depressed Offspring from 19–24 as a Function of Parental Depression.

	Maternal MDD				Paternal MDD			
	Female		Male		Female		Male	
Offspring variable	**Absent**	**Present**	**Absent**	**Present**	**Absent**	**Present**	**Absent**	**Present**
Dichotomous measures								
%MDD recurrence	47.4	54.5						
%Bipolar disorder	1.1	1.3						
%Suicide attempt	5.3	5.3						
%Anxiety disorder	7.4	14.3						
%Substance use	20.0	22.1						
Continuous measures								
MDD chronicity *M(SD)*	11.3 (21.7)	15.6 (25.4)						
MDD severity *M(SD)*	4.8 (3.2)	5.5 (3.2)						
Suicidal ideation *M(SD)*	0.4 (0.9)	0.4 (0.9)						
GAF *M(SD)*	77.4 (9.3)	76.3 (9.3)						

Note. MDD = major depressive disorder; GAF = Global Assessment of Functioning; *M* = mean; *SD* = standard deviation.

Table 2

Models Testing the Association of Parental MDD with Psychopathology and Functioning in Offspring from 19–24.

Offspring variable	Maternal MDD				Paternal MDD			
	Model 1	*p*-value	Model 2	*p*-value	Model 1	*p*-value	Model 2	*p*-value
Dichotomous measures								
MDD recurrence	1.33 (1.03–1.72)	.029	1.37 (1.04–1.80)	.025	1.16 (0.88–1.54)	.281	1.08 (0.80–1.44)	.618
Bipolar disorder	0.82 (0.24–2.70)	.743	0.66 (0.19–2.35)	.524	2.04 (0.61–7.14)	.248	1.90 (0.53–6.76)	.321
Suicide attempt	0.77 (0.45–1.33)	.354	0.69 (0.39–1.22)	.199	1.56 (0.94–2.63)	.084	1.70 (0.98–2.94)	.059
Anxiety disorder	1.75 (1.10–2.86)	.019	1.67 (1.01–2.76)	.044	1.49 (0.94–2.33)	.085	1.30 (0.80–2.11)	.289
Substance use	0.94 (0.70–1.27)	.691	0.92 (0.67–1.26)	.615	1.30 (0.28–5.88)	.099	1.31 (0.95–1.80)	.100
Continuous measures								
MDD chronicity	.15	.021	.14	.027	.07	.296	.03	.637
MDD severity	.13	.037	.10	.101	.10	.093	.05	.393
Suicidal ideation	.03	.682	.00	.956	.08	.188	.07	.291
GAF	−.14	.032	−.06	.262	−.15	.018	.08	.243

Note. MDD = major depressive disorder; GAF = Global Assessment of Functioning. Model 1 adjusts for the source of parental diagnostic data; Model 2 adjusts for (a) MDD in the co-parent, (b) whether the offspring had been living with the parent at T1, (c) non-mood disorder in the offspring by age 19, (d) parental non-mood disorder, and (e) whether the offspring was in a current episode of MDD at T3. Dichotomous outcomes are evaluated with odds ratios (and 95% confidence intervals); continuous outcomes are evaluated with semi-partial correlations.

J Abnorm Psychol. Author manuscript; available in PMC 2006 February 6.