Specific Parental Depression Symptoms as Risk Markers for New-Onset Depression in High-Risk Offspring

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ABSTRACT

Objective: To disaggregate the depression construct and investigate whether specific depression symptoms in parents with a history of recurrent depression are clinical risk markers for future depression in their high-risk offspring. Our hypothesis was that parental symptoms of the type that might impact offspring would most likely be of greatest importance.

Method: Data were drawn from a longitudinal high-risk family study. Families were mainly recruited from primary care and included 337 parent-child dyads. Parents had a history of recurrent *DSM-IV* unipolar depression and were aged 26–55 years. Their offspring (197 female and 140 male) were aged 9–17 years. Three assessments were conducted between April 2007 and April 2011. Ninety-one percent of families (n = 305) provided full interview data at baseline and at least 1 follow-up, of which 291 were included in the primary analysis. The main outcome measure was new-onset *DSM-IV* mood disorder in the offspring, which was assessed using the Child and Adolescent Psychiatric Assessment.

Results: Of the 9 *DSM-IV* depression symptoms, parental change in appetite or weight, specifically loss of appetite or weight, most strongly predicted new-onset mood disorder (odds ratio [OR] = 4.47; 95% CI, 2.04–9.79; $P < .001$) and future depression symptoms in the offspring (β = 0.12; $B = 0.21$; 95% CI, 0.00–0.42; $P = .050$). The cross-generational association was not accounted for by measures of parental depression severity (total depression symptom score, episode recurrence, age at onset, and past impairment or hospitalization) or other potential confounds (parent physical health, eating disorder, or medication).

Conclusions: Findings from this study suggest that loss of appetite or weight in parents with a history of recurrent depression is a marker of risk for depression in their offspring. The findings highlight the importance of examining depression heterogeneity. The biological and environmental mechanisms underlying this finding require investigation.

J Clin Psychiatry 2013;74(9):925–931

Submitted: *September 6, 2012; accepted January 10, 2013 (doi:10.4088/JCP.12m08152).*

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Parental depression is one of the best established risk factors for depression in young people.[1] Family studies have typically examined offspring risk according to parental depression diagnosis or total symptom scores. However, depression shows substantial heterogeneity in its presentation. Although research has examined whether parental age at onset of depression, chronicity, and severity differentially predict risk of illness in offspring,[2–5] studies investigating specific parental depression symptoms are rare.

Within-generation twin studies[6,7] of adult and juvenile depression have shown that some depressive symptoms are more heritable than others. There has been evidence suggesting that vegetative symptoms (changes in appetite, weight, or sleep) or those that reflect physiologic functions, such as loss of appetite, show the greatest heritability.[6,7] Specific depression symptoms have also been shown to influence overall familial liability to the disorder. Leckman et al[8] found that rates of major depressive disorder (MDD) were doubled among first-degree relatives of depressed probands who reported symptoms of appetite disturbance and excessive guilt as compared with relatives of depressed individuals who lacked these symptoms. To date, however, no study has explicitly examined whether there are differences in risk for offspring depression associated with specific depression symptoms in parents.

Although twin and family studies of adult depression suggest that the vegetative symptoms of depression are especially heritable, genetically informative cross-generational designs highlight the importance of noninherited environmental risk factors in the intergenerational transmission of depression.[9–12] Depressive symptoms that impact quality of relationships, such as loss of interest, could be thought to contribute to the development of depression via environmentally mediated effects, although this hypothesis has not been tested. A greater understanding of the risk associated with individual parental depression symptoms may help elucidate the mechanisms of intergenerational transmission, which at present are not well understood.[1,13] Such an approach could also give clues as to intervention and/or prevention targets in this high-risk group of children.[13] This goal is an important one given the severe long-term morbidity associated with depression in young people.[14–16] For example, if loss of interest and disengagement of the parent from his or her child were found to be risk factors, this finding might suggest that intervention efforts could be usefully directed at the quality of parent-child engagement.

This study utilizes data from a longitudinal study[3] of the offspring of recurrently depressed parents. Our aim was to investigate whether particular depression symptoms in parents are clinical risk markers of future depression in their offspring. We hypothesized that parental depression symptoms of the type that might impact offspring, eg, loss of interest, would most likely be of greatest importance.

Clinical Points

- Clinicians should be vigilant to the possibility of depression in the offspring of depressed parents.
- Parental depression as a risk to offspring may be influenced by heterogeneity in parental depression features.
- Parental loss of appetite or weight appears to be a particularly important marker of risk for future depression in offspring.

METHOD

Sample

The Early Prediction of Adolescent Depression study[3] is a prospective study of the high-risk offspring of recurrently depressed parents. Families were recruited predominantly from primary care (78%) and included 337 parents (315 mothers and 22 fathers, aged 26–55 years; mean age = 41.7 years, standard deviation [SD] = 5.5 years) with a clinical history of recurrent unipolar depression (at least 2 depressive episodes confirmed at interview) and one of their offspring (197 were female and 140 were male; age, 9–17 years; mean age = 12.4 years, SD = 2.0 years). When there was more than 1 child in the household who was willing to participate, the youngest eligible child was chosen for the study. Detailed information about sample recruitment and inclusion/exclusion criteria is included in Figure 1 and has been previously described.[3] Assessments of parents and offspring were conducted at 3 time points between April 2007 and April 2011. The mean time between assessments was 16 months (SD = 2.69 months) and 13 months (SD = 1.56 months), respectively. Ninety-one percent of families (n = 305) provided full interview data at baseline and at least 1 follow-up assessment. Families with interview data at follow-up did not differ from those who participated only at baseline with regard to parent or offspring baseline depression symptoms. Ethics approval for the study was obtained from the Multicenter Research Ethics Committee for Wales. Parents provided written consent, and their offspring provided assent at each assessment.

Measures

Offspring diagnosis and depression scores. The Child and Adolescent Psychiatric Assessment (CAPA) parent and child versions[17,18] were used to assess *DSM-IV* mood disorder (major depressive disorder, dysthymia, depressive disorder not otherwise specified, bipolar disorder, cyclothymia, or adjustment disorder with depressed mood) and number of *DSM-IV* depression symptoms (maximum of 9) in each offspring at each assessment. The CAPA is a semistructured diagnostic interview developed in accordance with *DSM-IV* and *ICD-10* criteria and has to be administered by trained interviewers who collect information on the onset, duration, frequency, and intensity of symptoms of a wide range of psychiatric disorders. It can be used to generate both dimensional symptom counts and psychiatric diagnoses. Most CAPA symptoms are scored on a 3-point scale (0, 2, 3), with symptoms considered present if given an intensity rating of 2 or greater. The presence of impairment resulting from psychiatric symptoms is also assessed across multiple domains of functioning. The CAPA is widely used in studies of child psychopathology and has been shown to be a reliable instrument.[17,18]

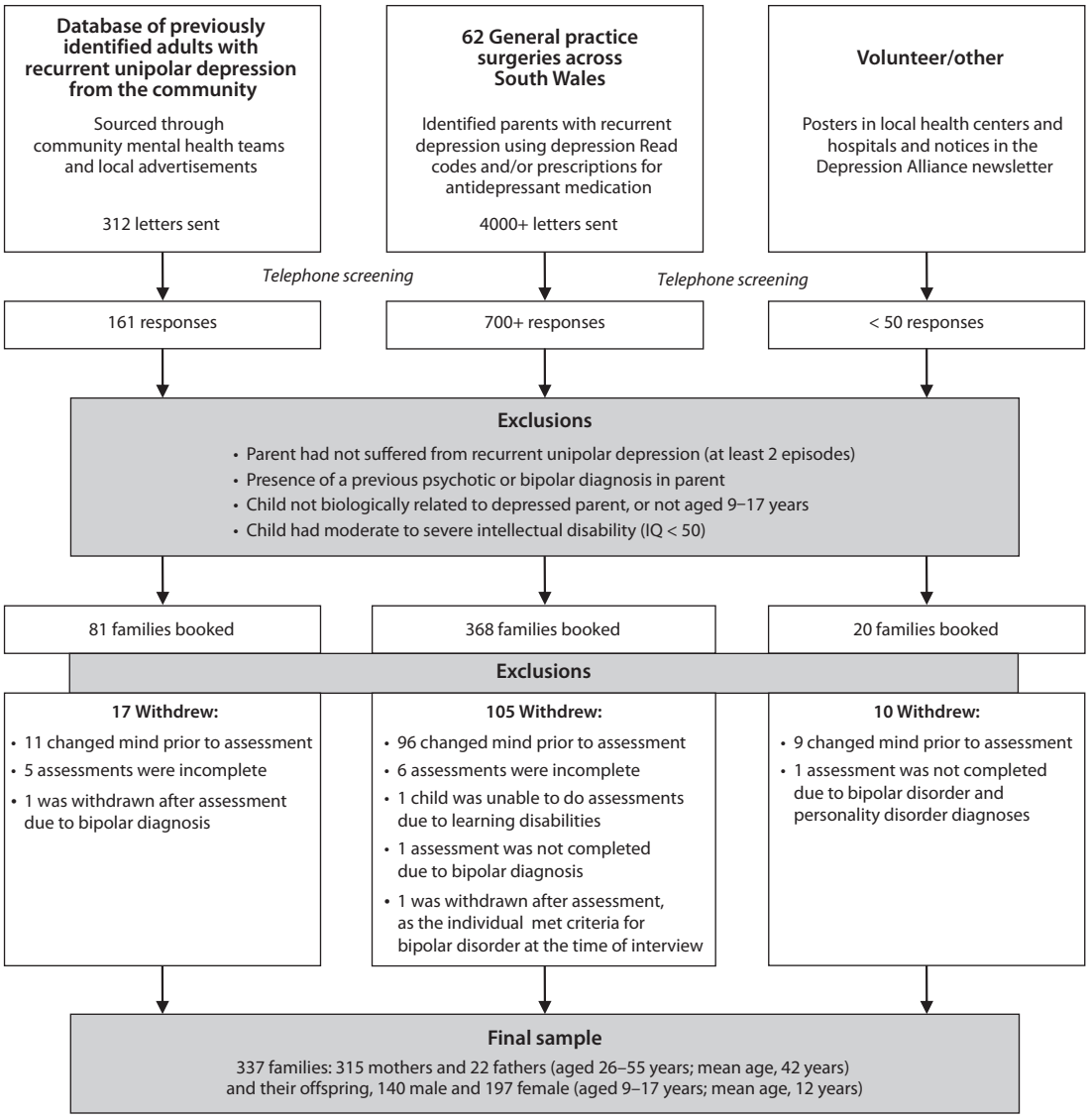
Offspring mood disorders were considered to be present if a diagnosis was made on the basis of either the parent or offspring interview.[18] All diagnoses and subthreshold cases were reviewed by 2 child psychiatrists. The main outcome measure was new-onset mood disorder in the offspring at either time point 2 or time point 3. For these analyses, to ensure that assessed parental symptoms preceded the disorder in the offspring, the small number of children and adolescents with a baseline diagnosis of mood disorder (14 of 305) were removed, leaving a final sample of 291 families.

Parent and offspring reports were also used to produce a total symptom count. Offspring depression symptom score at the final assessment was the secondary outcome measure. Mean imputation was used to generate symptom counts when there was 1 missing value. To address positive skew, symptom counts were transformed using a natural log transformation.

Parental depression symptoms. The Schedules for Clinical Assessment in Neuropsychiatry[19] (SCAN) was used at each time point to assess parental *DSM-IV* MDD diagnosis and depression symptoms occurring over the previous month. The SCAN is a set of instruments and manuals aimed at assessing, measuring, and classifying psychopathology and behavior associated with the major psychiatric disorders in adult life. It was developed within the framework of the World Health Organization and is compatible with both the *ICD-10* and *DSM-IV* classification systems. Responses are matched against the symptom definitions in the glossary and then rated by the interviewer for severity. Most SCAN items are coded according to the following criteria: symptom not present (coded as 0); symptom present but below the required threshold (coded as 1); symptom present to a moderate degree, or symptom severe but present for less than half of the time (coded as 2); and symptom present to a severe degree and present for more than half the time (coded as 3). For the present analyses, a symptom was required to be of at least moderate severity to be considered present. The presence or absence of individual depression symptoms was assessed and used to generate a psychiatric diagnosis of MDD according to *DSM-IV* criteria. The SCAN interviews were undertaken by trained interviewers and were supervised by a clinical psychiatrist who also reviewed diagnoses.

All parents had experienced at least 2 episodes of depression. Twenty-three percent of parents (68 of 291) met criteria for a depressive episode at the time of the baseline assessment. Fifty-eight percent of parents (120 of 207; data were incomplete for total depression symptoms at baseline for 16 parents) who did not meet criteria for MDD at baseline interview reported at least 1 depressive symptom during the

Figure 1. Study Recruitment Chart



preceding month. Each of the 9 *DSM-IV* criteria for MDD at baseline were tested as independent variables. Specific symptoms were endorsed by 8% (23 of 291 for retardation) to 45% (122 of 270 for sleep) of parents.

Parental depression symptoms were also assessed using the Beck Depression Inventory (BDI).[20] The BDI is a self-report questionnaire consisting of 21 questions, each scored on a scale of 0 to 3. Higher scores indicate greater depression severity. The BDI was included as part of a questionnaire battery that was sent out to families 2 weeks prior to the assessment.

Parental depression features. Information about prior depressive episodes was obtained retrospectively at baseline using a life history calendar approach,[21,22] which confirmed parental history of recurrent depression and provided information about age at depression onset, impairment during the worst 2 episodes (using the Global Assessment of Functioning [GAF] scale[23]), and any periods of hospitalization for depression. This approach was also used at time points 2 and 3 to assess any depressive episodes that occurred between assessments.

Further recurrence of parental depression over the course of the study. Depression recurrence was defined as a new episode of depression during the study period, including parents who met *DSM-IV* diagnostic criteria for depression (using the SCAN) either at follow-up interview or between the assessments. Sixty-five percent of parents (190 of 291) experienced episode recurrence.

History of severe, impairing parental depression. In accordance with previous research,[2,3] a severe depressive episode was defined as an episode that involved severe impairment (GAF score of ≤ 30) or hospitalization due to depression. Twenty-seven percent of parents (78 of 291) had experienced a severe depressive episode prior to the baseline assessment.

Age at parental depression onset. The mean age at depression onset in the parent sample was 26 years (SD = 8.3 years; range, 7–48 years).

Statistical Analysis

Logistic regression analyses tested associations between specific parental depression symptoms at baseline and new-onset mood disorder in the offspring. Primary analyses were conducted using baseline parental symptoms so that the parental symptoms preceded the offspring mood disorder. Symptoms that were significantly associated with offspring mood disorder were then examined using further multivariate analysis while covarying for the parent's total depression score.

Linear regression analyses tested associations between parental depression symptoms at baseline and the offspring depression symptom count at time point 3 as a secondary outcome measure. This analysis included the subsample of families who participated at baseline and time point 3 (n = 283). All analyses controlled for offspring age (at baseline) and gender and their interaction.

We further examined whether associations between parental depression symptoms and new-onset mood disorder in the offspring could be better explained by other features of parental depression course (age at depression onset, prior-episode impairment or hospitalization, and future episode recurrence).

Table 1. Univariate Associations Between Baseline Parental Depression Symptoms and New-Onset Mood Disorder in Offspring (n = 37)[a]

Baseline Parental Depression Symptom (N = 291)[b]	OR (95% CI)	*P* Value
Low mood (n = 107, 36.8%)	1.59 (0.79–3.22)	.19
Loss of interest or anhedonia (n = 84, 28.9%)	1.35 (0.65–2.83)	.42
Loss of energy (n = 67, 23.0%)	1.67 (0.78–3.57)	.19
Change in appetite or weight (n = 90, 31.3%)	3.21 (1.56–6.59)	.002
Change in sleep (n = 122, 45.2%)	1.95 (0.94–4.06)	.07
Low self-esteem or guilt (n = 103, 37.7%)	1.53 (0.75–3.12)	.24
Suicidality (n = 39, 14.2%)	1.24 (0.47–3.26)	.66
Retardation (n = 23, 7.9%)	0.97 (0.27–3.48)	.96
Loss of concentration or indecisiveness (n = 67, 23.0%)	2.47 (1.18–5.20)	.02

[a]The analysis was adjusted for offspring age and sex and their interaction, measured at baseline.
[b]Some percentages vary due to missing data.

Table 2. Multivariate Model Predicting New-Onset Mood Disorder in Offspring (n = 37)[a]

Parental Depression Symptom	OR (95% CI)	*P* Value
Change in appetite or weight	2.99 (1.35–6.61)	.007
Loss of concentration or indecisiveness	1.86 (0.67–5.16)	.24
Remaining *DSM-IV* depression symptoms (total score, maximum of 7 items)	0.94 (0.75–1.18)	.60

[a]The analysis was adjusted for offspring age and sex and their interaction, measured at baseline. The R^2 value is 0.056.

RESULTS

Description of Outcomes in Offspring

Rates of mood disorder in the offspring rose over the course of the study, from 4.6% (14 of 305) at baseline to 9.8% (28 of 287) at time point 2 and 9.9% (28 of 283) at time point 3. Excluding those children and adolescents with a mood disorder at baseline, 12.7% (37 of 291) developed a new-onset mood disorder at time point 2 or time point 3. The mean number of offspring *DSM-IV* depression symptoms reported at time point 3 was 2.0 (SD = 2.0; range, 0–9).

Parental Symptoms as Predictors of New-Onset Mood Disorder in the Offspring

The mean number of parental *DSM-IV* depression symptoms at baseline was 2.5 (SD = 2.6; range, 0–9). Both the total parental depression symptom count from the SCAN interview and the parent's score on the BDI were associated with increased risk for new-onset mood disorder in the offspring: SCAN symptom total: odds ratio (OR) = 1.14; 95% CI, 1.00–1.29; *P* = .04; BDI total: OR = 1.49; 95% CI, 1.00–2.22; *P* = .05. We next separately tested each of the 9 SCAN-rated *DSM-IV* depression symptoms (Table 1). Of the specific parental depression symptoms at baseline, only change in appetite or weight (OR = 3.21; 95% CI, 1.56–6.59; *P* = .002) and change in concentration or indecisiveness (OR = 2.47; 95% CI, 1.18–5.20; *P* = .017) significantly predicted new-onset mood disorder in the offspring. The association between parental appetite or weight change and new-onset mood disorder in the offspring remained significant after Bonferroni correction for multiple testing (9 tests; significant adjusted *P* value of < .005).

We further tested the extent to which the association between total parental depression symptom count and new-onset mood disorder in the offspring was accounted for by (1) appetite or weight change and (2) loss of concentration or indecisiveness. When these 2 items were removed from the total score, this variable (consisting of the remaining 7 *DSM-IV* items) no longer predicted new-onset mood disorder in the offspring (OR = 1.12; 95% CI, 0.95–1.31; *P* = .177). Multivariate analysis that included appetite or weight change, loss of concentration or indecisiveness, and parental total depression score as predictors revealed appetite or weight change to be the only significant predictor (Table 2).

Secondary Outcome: Depression Symptom Count in the Offspring at Time Point 3

A similar pattern of results was found for offspring depression symptom scores at final follow-up. Parental appetite or weight change (β = 0.17; *B* = 0.25; 95% CI, 0.09–0.41; *P* = .003), change in concentration or indecisiveness (β = 0.13; *B* = 0.20; 95% CI, 0.02–0.37; *P* = .027), and loss of interest or anhedonia (β = 0.11; *B* = 0.17; 95% CI, 0.00–0.33; *P* = .049) at baseline predicted future depression symptoms in the offspring (Table 3). Change in appetite or weight remained significant after Bonferroni correction for multiple testing (9 tests; significant adjusted *P* value of < .005) and was the only symptom that remained associated with future depression symptoms in the offspring in the multivariate analysis (Table 4).

Table 3. Univariate Associations Between Baseline Parental Depression Symptoms and Depression Symptoms in Offspring at Follow-Up[a]

Baseline Parental Depression Symptom (N = 283)[b]	β	*B*	95% CI	*P* Value
Low mood (n = 98, 34.6%)	0.03	0.04	−0.11 to 0.20	.58
Loss of interest or anhedonia (n = 81, 28.6%)	0.11	0.17	0.00 to 0.33	.05
Loss of energy (n = 66, 23.3%)	0.10	0.15	−0.03 to 0.32	.10
Change in appetite or weight (n = 84, 29.9%)	0.17	0.25	0.09 to 0.41	.003
Change in sleep (n = 112, 42.7%)	0.10	0.13	−0.03 to 0.29	.11
Low self-esteem or guilt (n = 96, 36.4%)	0.05	0.07	−0.09 to 0.23	.40
Suicidality (n = 37, 13.9%)	−0.02	−0.05	−0.27 to 0.18	.69
Retardation (n = 22, 7.8%)	0.08	0.18	−0.09 to 0.46	.19
Loss of concentration or indecisiveness (n = 68, 24.0%)	0.13	0.20	0.02 to 0.37	.03

[a]The analysis was adjusted for offspring age and sex and their interaction, measured at baseline.
[b]Some percentages vary due to missing data.

Table 4. Multivariate Models Predicting Depression Symptoms in Offspring at Follow-Up[a]

Parental Depression Symptom	β	*B*	95% CI	*P* Value
Change in appetite or weight	0.16	0.22	0.05 to 0.40	.01
Loss of concentration or indecisiveness	0.09	0.13	−0.11 to 0.37	.29
Loss of interest or anhedonia	0.09	0.13	−0.10 to 0.36	.27
Remaining *DSM-IV* depression symptoms (total score, maximum of 6 items)	−0.08	−0.03	−0.09 to 0.04	.37

[a]The analysis was adjusted for offspring age and sex and their interaction, measured at baseline. The R^2 value is 0.094.

Direction of Change in Parental Appetite or Weight

Clinical interview data allowed us to separately examine parental increase in appetite or weight (n = 35) and parental loss of appetite or weight (n = 46). Nine parents reported fluctuating or inconsistent symptoms and were not included in the analysis. Further analysis revealed no significant association between increase in appetite or weight and new-onset mood disorder (OR = 0.93; 95% CI, 0.31–2.85; *P* = .903) or future depression symptoms (β = 0.09; *B* = 0.17; 95% CI, −0.05 to 0.39; *P* = .132) in the offspring. In contrast, loss of appetite or weight was significantly associated with new-onset mood disorder in the offspring (OR = 4.47; 95% CI, 2.04–9.79; *P* < .001); 30% of the offspring whose parents reported loss of appetite or weight at baseline experienced a new-onset mood disorder at follow-up compared with only 9 percent of the offspring whose parents did not report loss of appetite or weight. Loss of appetite or weight in parents was also associated with future depression symptoms in the offspring (β = 0.12; *B* = 0.21; 95% CI, 0.00–0.42; *P* = .050).

Further sensitivity analysis revealed that parental loss of appetite or weight measured at the second assessment again prospectively predicted depression symptoms in the offspring at final follow-up (β = 0.13; *B* = 0.28; 95% CI, 0.03–0.52; *P* = .027) and showed a trend in the same direction for mood disorder (OR = 2.73; 95% CI, 0.90–8.31; *P* = .077). In contrast, parental increase in appetite or weight at time point 2 was not associated with either outcome in the offspring (*P* > .600).

Adjusting for Other Features of Parental Depression

Finally, we tested whether the observed associations between parental loss of appetite or weight and new-onset mood disorder in the offspring could be better accounted for by age at onset, past severity, or future recurrence of parental depression. Loss of appetite or weight was significantly associated with a younger age at onset of parental depression (OR = 0.94; 95% CI, 0.90–0.98; *P* = .003) and recurrence of parental depression at follow-up (OR = 3.40; 95% CI, 1.46–7.93; *P* = .005), but not past depression impairment or hospitalization (OR = 1.53; 95% CI, 0.78–3.00; *P* = .216). None of these parental depression features were, however, associated with new-onset mood disorder in the offspring (age at onset: OR = 0.97; 95% CI, 0.93–1.01; *P* = .151; depression recurrence: OR = 1.30; 95% CI, 0.61–2.77; *P* = .497; past impairment or hospitalization: OR = 1.56; 95% CI, 0.74–3.28; *P* = .238).

Association between parental loss of appetite or weight and new-onset mood disorder in the offspring was also not accounted for by parental antidepressant medication use, presence of long-term physical health problems, or eating disorder (results available upon request from the authors). The pattern of association between loss of appetite or weight and new-onset mood disorder in the offspring was similar when only mothers (270 of 291 parents) were included in the analysis (OR = 3.64; 95% CI, 1.60–8.26; *P* = .002); when parents who met *DSM-IV* depression criteria at baseline assessment were excluded (OR = 4.77; 95% CI, 1.44–15.76; *P* = .010); when children or adolescents with a new-onset diagnosis of bipolar disorder, cyclothymia, or adjustment disorder were excluded (8 of 37 new-onset mood disorder diagnoses; OR = 3.50; 95% CI, 1.45–8.48; *P* = .005), and when specific parental symptoms were derived from questionnaires (ie, the BDI) rather than interviews (OR = 2.55; 95% CI, 1.25–5.21; *P* = .010).

DISCUSSION

Depression symptom heterogeneity is widely recognized but rarely investigated, particularly in relation to offspring risk for depression. Within this high-risk sample, our findings suggest that specific parental depression symptoms differentially predict risk for future new-onset mood disorder in the offspring. Parental loss of appetite or weight emerged as a particularly important marker of risk: 30% of the offspring whose parents reported baseline loss of appetite or weight experienced a new-onset mood disorder at follow-up, compared with only 9 percent of the offspring whose parents did not report loss of appetite or weight. This association remained after accounting for parental overall level of depression symptoms. Moreover, removing appetite or weight change from the total symptom count removed the association with new-onset mood disorder, suggesting that this item was contributing substantially to the initial observed relationship.

Parental loss of appetite or weight is a feature that many would consider unlikely to have a direct negative impact on offspring; however, our finding that this symptom appears to be an especially important marker of offspring depression risk is consistent with evidence from family and twin studies. For example, Leckman et al[8] found that appetite disturbance was the symptom most discriminative of MDD in relatives of depressed probands, and appetite or weight disturbance has been previously highlighted as a symptom associated with greater depression severity.[24] On balance, research[6,7,25] suggests that the vegetative symptoms (including appetite and weight disturbance) also appear to be more heritable than the other depression symptoms.

Depression with an early age at onset is also thought to be associated with increased familial aggregation and greater heritability than depression with an onset later in life.[4,26] In this study, parental loss of appetite or weight was associated with a younger age at onset in parents. Thus, this symptom may be a marker for a stronger genetic liability to early-onset depression, not only in parents but also in offspring. However, loss of appetite or weight could also be a marker of some additional unmeasured variable that has environmental effects on offspring.

We originally hypothesized that parental depression symptoms that might have the greatest psychosocial impact on offspring, such as loss of interest, would be the most important predictors. We did not find evidence in favor of this hypothesis in this high-risk child and adolescent sample. Although parents who are depressed have been shown to be more disengaged, withdrawn, and less responsive in their interactions with their children,[27–29] the majority of research has been conducted with infants or preschool-aged children. Findings from twin research suggest that the influence of genetic factors on depression symptoms increases in adolescence, while the importance of the family environment diminishes. This increase is possibly due to an increase in gene-environment correlation as adolescents become more autonomous and more able to seek out and shape their own environments.[30,31] Thus, it is possible that, during this developmental stage, offspring depression risk may be better indexed by the more heritable symptoms in parents, even though environmental factors also contribute. In addition, the impact of proximal, environmentally mediated parental depression symptoms may be reduced as adolescents spend more time outside of the family home.

Although parental loss of appetite or weight appears to be an important marker of risk, we can only speculate as to the mechanisms that might be involved. Appetite regulation and depression share some common neurochemical and neurophysiologic underpinnings.[32–37] For example, serotonergic pathways[34–35,37] and the hypothalamic-pituitary-adrenal axis[32,36] are systems that are involved in the regulation of appetite and have also been linked to depression. Thus, loss of appetite or weight may represent a core underlying feature of depression vulnerability. However, it is also possible that loss of appetite or weight may be a marker of unmeasured environmental adversity.

Strengths and Limitations

Very few studies have considered which features of parental depression are the best predictors of future onset of depression in offspring. The current 4-year longitudinal study featured very high rates of retention and involved multiple informants and multiple measures of offspring depression derived from diagnostic interviews. Several potential confounding factors were also addressed. The findings must, however, be interpreted in light of several study limitations. The number of offspring with new-onset mood disorder in this sample was small (n = 37), which may have limited the power to detect smaller effect sizes. However, similar results were found when we used the offspring depression symptom count as our outcome measure. The small number of offspring with new-onset mood disorder also precluded our ability to examine associations separately according to offspring age and gender, which may be important moderators of intergenerational depression risk. For example, cross-generational environmental links appear to be stronger between mothers and daughters.[12] As the majority of parents participating in the study were mothers (270 of 291), we were unable to examine associations separately according to parent gender. Sensitivity analysis including only mothers generated a similar pattern of results; however, the subgroup of fathers was too small to analyze separately, and we are therefore unable to generalize our findings to offspring of depressed fathers.

The focus of this investigation was on the depression symptoms that compose the *DSM-IV* diagnosis of MDD. There are, however, other depression-related symptoms not captured by these diagnostic criteria (eg, irritability, impaired functioning, or social withdrawal) that may be important in indexing depression risk in offspring. Parental comorbidity, which was shown in our previous study[38] to be associated with child psychopathology, was also not examined.

Some studies, eg, Oquendo et al,[39] have suggested that symptoms are variable across depressive episodes. However, other researchers[25,40] have found symptom presentations to be similar, and, in the present study, correlation coefficients for parental loss of appetite or weight were highly significant across depressive episodes ($P < .001$). Moreover, sensitivity analysis that looked at parental loss of appetite or weight at time point 2 showed a consistent pattern of findings.

In addition, the present study focused on an important clinical sample: parents with a history of recurrent depression, who, although identified from primary care, were more likely to be a much more severely affected group than population-based samples. It is plausible that risk markers for depression symptoms in offspring in the general population are not the same as those for depressive disorder in offspring in high-risk families. If this possibility were the case, then it would highlight the need for both clinically informative samples such as the one used in the present study, as well as population-based studies.

Summary

The present study identified parental loss of appetite or weight as an important marker of risk for future depression in

offspring. Although there are some plausible biological links, it is unlikely that parental loss of appetite or weight itself would have a direct negative impact on offspring. Further research is therefore required to identify and characterize the genetic, familial, social, and biological mechanisms that might explain the link between parental loss of appetite or weight and depression risk in offspring.

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Potential conflicts of interest: None reported.

Funding/support: The adolescent depression study was supported by the Sir Jules Thorn Charitable Trust, London, United Kingdom. Dr A. K. Thapar was supported by the National Institute for Social Care and Health Research, Cardiff, United Kingdom. Dr Collishaw was supported by the Waterloo Foundation, Cardiff, United Kingdom. The sponsors had no further role in the study design; the collection, analysis, and interpretation of data; manuscript preparation; or the decision to submit the manuscript for publication.

Acknowledgments: We are very grateful to all the families who participated in this study. We thank Robert Potter, MRCPsych (of the Institute of Psychological Medicine and Clinical Neurosciences, MRC Centre for Neuropsychiatric Genetics and Genomics, Neuroscience and Mental Health Research Institute, Cardiff University, Cardiff, United Kingdom), and Daniel Smith, MD, MRCPsych (of the University of Glasgow, Glasgow, Scotland), who helped with supervising the clinical assessments. We also thank Anthony Isles, PhD (of the Institute of Psychological Medicine and Clinical Neurosciences, MRC Centre for Neuropsychiatric Genetics and Genomics, Neuroscience and Mental Health Research Institute, Cardiff University, Cardiff, United Kingdom) and Sir Michael Rutter, MD, FRS, FRCPsych, FBA, FAcMedSci; Barbara Maughan, PhD; and Andrew Pickles, PhD (all of Kings College London, London, United Kingdom) for their helpful comments and advice. These acknowledged individuals report no conflicts of interest.

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