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Familial aggregation of postpartum mood symptoms in bipolar disorder pedigrees

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Abstract

Objectives—We sought to determine if postpartum mood symptoms and depressive episodes exhibit familial aggregation in bipolar I pedigrees.

Methods—A total of 1,130 women were interviewed with the Diagnostic Interview for Genetic Studies as part of the National Institute of Mental Health (NIMH) Genetics Initiative Bipolar Disorder Collaborative Study and were asked whether they had ever experienced mood symptoms within four weeks postpartum. Women were also asked whether either of two major depressive episodes described in detail occurred postpartum. We examined the odds of postpartum mood symptoms in female siblings, who had previously been pregnant and had a diagnosis of bipolar I,

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bipolar II, or schizoaffective (bipolar type) disorders (n = 303), given one or more relatives with postpartum mood symptoms.

Results—The odds ratio for familial aggregation of postpartum mood symptoms was 2.31 (p = 0.011) in an Any Mood Symptoms analysis (n = 304) and increased to 2.71 (p = 0.005) when manic symptoms were excluded, though this was not significantly different from the Any Mood Symptoms analysis. We also examined familial aggregation of postpartum major depressive episodes; however, the number of subjects was small.

Conclusions—Limitations of the study include the retrospective interview, the fact that the data were collected for other purposes and the inability to control for such factors as medication use. Taken together with previous studies, these data provide support for the hypothesis that there may be a genetic basis for the trait of postpartum mood symptoms generally and postpartum depressive symptoms in particular in women with bipolar disorder. Genetic linkage and association studies incorporating this trait are warranted.

Keywords

bipolar; genetics; postpartum

Postpartum depression is a serious syndrome which occurs in up to 10–20% of all mothers in the year following delivery (1, 2). While the etiology of postpartum depression is unknown, it is likely to be multifactorial with psychological factors, biological factors including hormonal changes, and social factors all playing a role. The risk for postpartum depression is increased in women with a history of major depression (3, 4), as well as in women with a history of postpartum depression following prior pregnancies (5, 6).

In women with bipolar disorder (BD), the risk of postpartum mood episodes (depression or mania) has been reported in up to 25–40% (7) and the risk of postpartum psychosis in particular (a syndrome resembling mania with psychotic features) in women with bipolar I disorder (BD I) has been reported to be 20–30% (8–10). There have been fewer studies specifically examining the rates of postpartum depressive episodes in women with BD. Freeman et al. (11) found that 67% of 30 women with BD experienced a postpartum mood episode within one month of childbirth, the majority of which were depressive episodes. Further, in eight of these women who had more than one child, the recurrence rate of a postpartum depressive episode was 100% in women who experienced postpartum depression after the birth of their first child (11).

The evidence that postpartum mood syndromes may have a genetic basis is supported by several studies. Treloar et al. (12) interviewed 838 parous female twin pairs and concluded that genetic factors explained 38% of the variance in postnatal depression. There have been several family studies of postpartum psychosis. These studies support the idea of a genetic susceptibility to a postpartum trigger, as well as an overlap in genetic factors predisposing to postpartum psychosis and bipolar illness (13, 14). Dean et al. (15) suggested a higher risk of postpartum mood illness in relatives of probands with postpartum psychosis. We recently reported familial aggregation of postpartum as well as perinatal depressive symptoms in families with recurrent early onset major depression (16). Similarly, Forty et al. (17) have

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shown that the trait of postpartum depression (with onset in ≤4 weeks postpartum) exhibited familiality in pedigrees with recurrent major depression. To our knowledge there has been no study of familial aggregation of postpartum depressive episodes in families with BD.

In this study, we sought to determine if postpartum mood symptoms generally, and postpartum depressive episodes in particular, show familial aggregation in BD pedigrees.

Methods

Sample

The sample consisted of women who participated in a multi-site genetics study of BD which was collected for the National Institute of Mental Health (NIMH) Genetics Initiative Bipolar Disorder Collaborative project. Johns Hopkins was part of a 10-site collaboration that collected this sample from 1999 to 2003. The additional sites were Indiana University, Washington University in St. Louis, the NIMH Intramural Program, the University of California, San Diego, University of Iowa, University of Pennsylvania, University of Chicago, Rush-Presbyterian Medical Center, and University of California, Irvine. Inclusion criteria focused on BD I probands with at least one sibling with BD I. A total of 53% of the affected subjects were female (18, 19). The sample was primarily Caucasian, with African-Americans comprising 5.5% of the total and Hispanics 1.9%.

Subjects were recruited through various means, including newspaper, magazine and radio advertising, as well as from clinical settings. After a complete description of the study had been given to the subjects, written informed consent was obtained. Diagnoses were based upon an interview conducted using the Diagnostic Interview for Genetic Studies (DIGS; see below) (20). Collateral information from family informants and medical records was obtained whenever possible. Final diagnoses were made at each site by two clinicians who reviewed all available data using a best-estimate diagnosis procedure based on the DSM-IV.

The final sample included 303 women derived from a total of 1,130 women. In the total sample, 105 had a diagnosis of major depressive disorder (MDD), 666 had BD I, 64 had bipolar II disorder (BD II), 24 had schizoaffective disorder, bipolar type (SABP), 123 had a non-affective diagnosis (e.g., an anxiety disorder) and 147 were relatives who had never been mentally ill. A total of 81.5% (n = 922) of the sample had had a previous pregnancy. Thus, there were 591 women with a diagnosis of BD I, BD II or SABP, and a previous pregnancy. Of these 591 women, we excluded 217 women whose families did not have another woman with BD who had also been pregnant and 71 women who were non-siblings, leaving 303 individuals from 139 families.

Interview

The DIGS 3.0 version (20) was used as part of the diagnostic process. Inter-rater reliability has been shown to be 0.85–0.96 for mood disorders (20). As part of the Medical Section, every woman was asked questions about mood symptoms during and after pregnancy. Specifically, each woman was asked: ‘Have you ever had any severe emotional problems during a pregnancy or within a month of childbirth?’ Clinicians were allowed flexibility in their interview in order to obtain enough information to accurately answer the questions.

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Affirmative answers allowed for a designation that included during pregnancy only, both during and after pregnancy, and after pregnancy only. Since we were interested in mood symptoms that may have been specifically triggered by the hormonal changes that occur during and after childbirth, we counted as positive for our analyses those women who answered 'after pregnancy only', excluding others who answered 'both during and after pregnancy'. A description of the types of symptoms that were experienced was included. In addition, each subject was asked to describe two major depressive episodes – the most severe episode and a second well-remembered episode. As part of this Depression Section of the interview, women were asked whether the described episode had occurred during or after pregnancy. In addition, the month and year of the onset of the major depressive episode and the month and year of the childbirth were collected. These dates again allowed us to include as positive for our analyses only those women whose depressive episode began at or after delivery of their child.

Statistical analysis

We examined demographics using either the two-tailed Student's *t*-test or the chi-square test when indicated. We used the two-tailed Student's *t*-test to compare the mean age of interview, age of onset of BD, number of major depressive episodes, number of manic episodes, longest depressive episode (in days), number of pregnancies, number of live births and years of education in the sample of women with and without a history of postpartum mood symptoms. Similarly, we used the chi-square test to compare the percentage of women currently depressed and currently married in women with and without a history of postpartum mood symptoms.

We used the generalized estimating equation (GEE) (21) to examine familial aggregation of the trait of postpartum mood symptoms. This approach uses logistic regression but also takes into account potential correlation between observations when multiple members of the same family are considered. We examined the odds of family history of postpartum mood symptoms positively predicting postpartum mood symptoms in the individual. A positive family history of postpartum mood symptoms was defined as having another member or members of the family who also gave a history of postpartum mood symptoms or depression, while a negative family history was defined as having no family members who gave a history of postpartum mood symptoms or depression by direct interview using the DIGS. For each analysis described below, the same criteria were used to assign a positive family history and to assign a positive individual history. We also examined rates, comparing: (i) the number of women who had postpartum symptoms and a family history of postpartum symptoms, divided by the total number of women with a family history of postpartum symptoms; and (ii) the number of women who had postpartum symptoms and NO family history of postpartum symptoms divided by the total number of women without a family history of postpartum symptoms. In these analyses, we used general family history of postpartum mood history to predict postpartum mood symptoms rather than proband history, since many of the probands in the family were either male or had never been pregnant. All analyses were carried out using STATA 9.0.

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We completed two sets of analyses. The first used information from the Medical Section examining the familiality of postpartum mood symptoms. This analysis has the advantage of being broadly inclusive, i.e., women indicated in this part of the interview if they had *ever* experienced severe emotional problems during or after pregnancy. The disadvantages of this analysis are that there is no information as to whether depressive symptoms met criteria for a major depressive episode, and that some of the episodes may have been manic or mixed. The second analysis used information from the Major Depression Section, in which two major depressive episodes were described. The advantage of this analysis is that we can be sure that the episode described met criteria for a major depressive episode; however, many postpartum episodes may be missed since each subject only described 2 of an average of about 20 episodes in their lifetime. Based on the Medical Section, we completed two analyses: (i) 'Any Mood Symptoms', in which the women included in the analysis were siblings (n = 303, 139 families) and were scored positive for answering yes to having postpartum mood symptoms; and (ii) 'Depression Only', in which women who experienced manic symptoms (as detailed in the Description field) were scored as negative for the trait of postpartum depressive symptoms. We scored as negative for postpartum symptoms women whose description included the words 'mania' or 'hypomania'. One woman was also scored as negative for a description of increased bulimic symptoms postpartum.

For the Major Depression Section, dates of the childbirth and onset of the described major depressive episode were compared and women were scored as positive for a postpartum depressive episode if the date of the childbirth preceded or coincided with the onset of the depressive episode. Because the dates were not exact (month and year only), we completed three sets of analyses: (i) One Month, in which episodes were scored as positive if the month of childbirth and the month of the onset of depressive episode were the same; (ii) Two Months, in which episodes were scored as positive if the childbirth took place the month before the onset of depression; and (iii) Three Months, when the month of childbirth and the onset of depression were ≤2 months apart. In this analysis, ≤3 months passed from the onset of delivery to the onset of the major depressive episode. Note that the Two-Months analysis included women who scored positive in the One-Month analysis and, similarly, the Three-Month analysis included women who scored positive in the One-Month and Two-Months analyses. This allowed us to examine familial aggregation based on the DSM definition of <4 weeks (represented by the One-Month analysis) as well as up to three months postpartum.

Results

Table 1 shows clinical and demographic characteristics of women with (n = 55) and without (n = 247) postpartum mood symptoms, as determined by the Medical Section in the entire sample (n = 303). There were no significant differences between women with and without these symptoms except for the number of live births and age at interview. Women with postpartum mood symptoms had significantly more live births compared to women without these symptoms and were also significantly older. Clinical characteristics such as age of onset, number of major depressive and manic episodes, and current depression did not differ significantly between the two groups.

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Table 2 shows the results of the familiality analyses based on the Medical Section. Since there was a significant difference in the number of live births and age at interview between women with and without postpartum mood episodes, we controlled for both these factors in the odds ratio analyses. The rate of women with postpartum symptoms and a positive family history of postpartum symptoms (30.43%) was higher than the rate of women with postpartum symptoms and a negative family history of postpartum symptoms (14.53%). This was reflected in a significant odds ratio of 2.31 ($p = 0.011$) for postpartum mood symptoms of any type in the Any Mood Symptoms analysis. The odds ratio increased to 2.71 ($p = 0.005$) when manic symptoms were excluded, though this was not significantly different from the Any Mood Symptoms analysis.

Table 3 displays the results of the familial analyses based on the Major Depression Section. Again, all analyses were controlled for numbers of live births and age at interview. We were limited by a very small sample size. Only 16 of 303 women classified one or both major depressive episodes described during the interview as postpartum (within three months postpartum). Nonetheless, in the One-Month analysis, episodes that occurred within one month postpartum had an odds ratio for familial aggregation of 5.79 ($p = 0.038$), which became non-significant when episodes occurring up to three months postpartum were included (odds ratio 3.96, $p = 0.094$). Note that the number of women who met the criteria for the Two-Months analysis was only two more than for the One-Month analysis and no additional women met the criteria for the Three-Months analysis. The rate of women with postpartum depressive episodes and a positive family history of postpartum depressive episodes was again higher than the rate of women with postpartum depressive episodes and a negative family history.

Discussion

To our knowledge this is the first study to examine the familiality of postpartum mood symptoms generally, as well as postpartum depressive episodes particularly, in women with BD. We found evidence that these symptoms and these episodes do aggregate in families. Our findings build on and extend previous work demonstrating similar clustering of postpartum depression in MDD (16, 17) pedigrees and of postpartum psychosis in BD pedigrees (13, 15). Our results provide additional evidence for a familial basis for mood symptoms with onset in the postpartum period in women with mood disorders.

There are a number of possible interpretations of our findings. The familiality of these symptoms may reflect a genetic vulnerability, though environmental influences are also possible. For example, a familial history of severe postpartum mood symptoms could influence the personal interpretation of the very common experience of postpartum blues, particularly in a woman with a pre-existing mood disorder. We were not able to distinguish between postpartum blues or more severe postpartum depression in the Medical Section of our data. Other non-genetic or environmental factors that have been proposed to be involved in the development of at least some episodes of postpartum depression include sleep deprivation (22–24), the stress of becoming a mother (25–28), and alterations in the hypothalamic–pituitary–adrenal (HPA) axis triggered by labor and delivery (29–32). On the other hand, even these seemingly environmental etiologies could have genetic components.

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For example, sleep deprivation could trigger postpartum depressive episodes in women who are genetically vulnerable to this type of stressor. The stress of labor, delivery and taking care of a young infant could trigger depression in those with a vulnerability conferred by, for example, one or two copies of the short allele of the serotonin transporter gene (33). Alterations in the HPA axis after labor and delivery might trigger depression in those with susceptibility variants in cortisol-related genes.

Another genetic mechanism of interest is the effect of estrogen on gene transcription in the brain (34). Estrogen is known to act through two different intracellular estrogen receptors, ER-α and ER-β, that reside in the nuclei of cells. These receptors are able to influence genomic transcription, which then directs or modulates the synthesis of enzymes, receptor proteins, and signal transduction enzymes. Recent work by Jones et al. (13), however, indicates no association between two polymorphisms in the ER-α gene and postpartum psychosis. Nonetheless, it remains unclear whether alterations in other genes that are influenced by estrogen are involved in the genetic basis of postpartum mood syndromes, as well as whether the underlying mechanism(s) for postpartum psychosis, are the same as those for postpartum depressive episodes.

Our finding that limiting positive episodes to depressive symptoms results in a larger odds ratio is difficult to interpret. The odds ratio improved; however, the confidence intervals overlap with those of the more general analysis. One possibility that remains to be explored is that familial aggregation of postpartum manic or psychotic episodes is separate from the familial aggregation of postpartum depressive episodes, indicating a different underlying mechanism. We cannot draw that conclusion from the data presented here, however.

We chose to focus on symptoms and episodes which began explicitly after labor and delivery. Recent evidence indicates that that some episodes of ‘postpartum’ depression actually begin during pregnancy (35). Mood episodes which begin during pregnancy or several months postpartum may conceivably have a very different biological basis than mood episodes which appear to be triggered shortly after the hormonal changes that occur during labor and delivery. The DSM-IV designates the use of the term ‘postpartum’ as mood episodes which occur within four weeks of labor and delivery. Although this time period remains controversial since the exact period of biological consequences secondary to hormonal withdrawal remains unknown (36), it is a reasonable starting point when attempting to examine more homogeneous ‘types’ of postpartum mood episodes, since mood episodes which begin within a month of labor and delivery are more likely to be associated with concurrent hormonal changes.

There are several important limitations to consider when interpreting our findings. First, the sample was originally collected for other purposes and thus the interview was not focused on obtaining the maximum level of detail about the relationship between childbirth and mood symptomatology. Thus, in the Major Depression Section, our analyses were limited to the small number of women who described in detail a postpartum depressive episode. While the women in the study had had an average of 20 lifetime major depressive episodes, only 2 were described in any detail for our interview. Further, the interview did not contain a question about whether manic or hypomanic episodes had their onset during or after

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pregnancy. A second limitation was the retrospective nature of the interview. A number of studies have found that the reliability of retrospective recall of mood-related symptomatology, such as premenstrual symptoms, is questionable (37–39). One issue with these studies is that they were, in general, attempting to confirm both timing and frequency of symptoms in order to make the retrospective diagnosis of premenstrual dysphoric disorder. To our knowledge, there have been no such studies examining the reliability of retrospective recall for postpartum mood episodes. One important difference between the recall of a postpartum episode and other types of mood symptoms, including premenstrual symptoms, is that the first involves a momentous event, the birth of a child, the date of which is remembered and to which other events, such as mood symptoms, can be tied. Nonetheless, prospective studies would likely provide more reliable data with which to address the familiality of postpartum mood symptoms. We were also not able to control for such factors as medication use during and after pregnancy (since these data were not collected), which may have influenced our results. Finally, we performed multiple comparisons and did not correct for this statistically.

In summary, these findings indicate that there may be a genetic basis for the trait of postpartum depressive symptoms in women with BD. Future genetic linkage and association studies will be needed to test molecular hypotheses about the biological underpinnings of this trait.

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References

1. Campbell SB, Cohn JF. Prevalence and correlates of postpartum depression in first-time mothers. J Abnorm Psychol 1991; 100: 594–599. [PubMed: 1757673]
2. Robinson GE, Stewart DE. Postpartum psychiatric disorders. CMAJ 1986; 134: 31–37. [PubMed: 3510069]
3. Kumar R, Robson KM. A prospective study of emotional disorders in childbearing women. Br J Psychiatry 1984; 144: 35–47. [PubMed: 6692075]
4. Frank E, Kupfer DJ, Jacob M, Blumenthal SJ, Jarrett DB.Pregnancy-related affective episodes among women with recurrent depression. Am J Psychiatry 1987; 144: 288–293. [PubMed: 3826425]
5. Cox JL, Murray D, Chapman G. A controlled study of the onset, duration and prevalence of postnatal depression. Br J Psychiatry 1993; 163: 27–31. [PubMed: 8353695]
6. Cooper PJ, Campbell EA, Day A, Kennerley H, Bond A.Non-psychotic psychiatric disorder after childbirth. A prospective study of prevalence, incidence, course and nature. Br J Psychiatry 1988; 152: 799–806. [PubMed: 3167466]
7. Hunt N, Silverstone T. Does puerperal illness distinguish a subgroup of bipolar patients? J Affect Disord 1995; 34: 101–107. [PubMed: 7665801]
8. Kendell RE, Chalmers JC, Platz C. Epidemiology of puerperal psychoses. Br J Psychiatry 1987; 150: 662–673. [PubMed: 3651704]
9. Bratfos O, Haug JO. Puerperal mental disorders in manic-depressive females. Acta Psychiatr Scand 1966; 42: 285–294. [PubMed: 5959091]

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10. Reich T, Winokur G. Postpartum psychoses in patients with manic depressive disease. J Nerv Ment Dis 1970; 151: 60–68. [PubMed: 5426650]
11. Freeman MP, Smith KW, Freeman SA et al. The impact of reproductive events on the course of bipolar disorder in women. J Clin Psychiatry 2002; 63: 284–287. [PubMed: 12004800]
12. Treloar SA, Martin NG, Bucholz KK, Madden PA, Heath AC. Genetic influences on post-natal depressive symptoms: findings from an Australian twin sample. Psychol Med 1999; 29: 645–654. [PubMed: 10405086]
13. Jones I, Middle F, McCandless F et al. Molecular genetic studies of bipolar disorder and puerperal psychosis at two polymorphisms in the estrogen receptor alpha gene (ESR 1). Am J Med Genet 2000; 96: 850–853. [PubMed: 11121195]
14. Jones I, Craddock N. Familiality of the puerperal trigger in bipolar disorder: results of a family study. Am J Psychiatry 2001; 158: 913–917. [PubMed: 11384899]
15. Dean C, Williams RJ, Brockington IF. Is puerperal psychosis the same as bipolar manic-depressive disorder? A family study. Psychol Med 1989; 19: 637–647. [PubMed: 2798633]
16. Murphy-Eberenz K, Zandi PP, March D et al. Is perinatal depression familial? J Affect Disord 2006; 90: 49–55. [PubMed: 16337009]
17. Forty L, Jones L, Macgregor S et al. Familiality of postpartum depression in unipolar disorder: results of a family study. Am J Psychiatry 2006; 163: 1549–1553. [PubMed: 16946179]
18. McInnis MG, Dick DM, Willour VL et al. Genome-wide scan and conditional analysis in bipolar disorder: evidence for genomic interaction in the National Institute of Mental Health Genetics Initiative Bipolar Pedigrees. Biol Psychiatry 2003; 54: 1265–1273. [PubMed: 14643094]
19. Dick DM, Foroud T, Flury L et al. Genomewide linkage analyses of bipolar disorder: a new sample of 250 pedigrees from the National Institute of Mental Health Genetics Initiative. Am J Hum Genet 2003; 73: 107–114. [PubMed: 12772088]
20. Nurnberger JI Jr, Blehar MC, Kaufmann CA et al. Diagnostic interview for genetic studies. Rationale, unique features, and training. NIMH Genetics Initiative. Arch Gen Psychiatry 1994; 51: 849–859. [PubMed: 7944874]
21. Zeger SL, Liang KY. Longitudinal data analysis for discrete and continuous outcomes. Biometrics 1986; 42: 121–130. [PubMed: 3719049]
22. Ross LE, Murray BJ, Steiner M. Sleep and perinatal mood disorders: a critical review. J Psychiatry Neurosci 2005; 30: 247–256. [PubMed: 16049568]
23. Dennis CL, Ross L. Relationships among infant sleep patterns, maternal fatigue, and development of depressive symptomatology. Birth 2005; 32: 187–193. [PubMed: 16128972]
24. Hiscock H, Wake M. Infant sleep problems and postnatal depression: a community-based study. Pediatrics 2001; 107: 1317–1322. [PubMed: 11389250]
25. Boury JM, Larkin KT, Krummel DA. Factors related to postpartum depressive symptoms in low-income women. Women Health 2004; 39: 19–34. [PubMed: 15256353]
26. O'Hara MW. Social support, life events, and depression during pregnancy and the puerperium. Arch Gen Psychiatry 1986; 43: 569–573. [PubMed: 3707289]
27. O'Hara MW, Schlechte JA, Lewis DA, Varner MW. Controlled prospective study of postpartum mood disorders: psychological, environmental, and hormonal variables. J Abnorm Psychol 1991; 100: 63–73. [PubMed: 2005273]
28. Seguin L, Potvin L, St-Denis M, Loiselle J. Socioenvironmental factors and postnatal depressive symptomatology: a longitudinal study. Women Health 1999; 29: 57–72.
29. Wisner KL, Stowe ZN. Psychobiology of postpartum mood disorders. Semin Reprod Endocrinol 1997; 15: 77–89. [PubMed: 9065980]
30. Harris B, Lovett L, Smith J, Read G, Walker R,Newcombe R. Cardiff puerperal mood and hormone study. III. Postnatal depression at 5 to 6 weeks postpartum, and its hormonal correlates across the peripartum period. Br J Psychiatry 1996; 168: 739–744. [PubMed: 8773817]
31. Bloch M, Rubinow DR, Schmidt PJ, Lotsikas A, Chrousos GP, Cizza G. Cortisol response to ovine corticotropinreleasing hormone in a model of pregnancy and parturition in euthymic women with and without a history of postpartum depression. J Clin Endocrinol Metab 2005; 90: 695–699. [PubMed: 15546899]

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32. Hendrick V, Altshuler LL, Suri R. Hormonal changes in the postpartum and implications for postpartum depression. Psychosomatics 1998; 39: 93–101. [PubMed: 9584534]

33. Caspi A, Sugden K, Moffitt TE et al. Influence of life stress on depression: moderation by a polymorphism in the 5-HTT gene. Science 2003; 301: 386–389. [PubMed: 12869766]

34. McEwen B Estrogen actions throughout the brain. Recent Prog Horm Res 2002; 57: 357–384. [PubMed: 12017552]

35. Stowe ZN, Hostetter AL, Newport DJ. The onset of postpartum depression: implications for clinical screening in obstetrical and primary care. Am J Obstet Gynecol 2005; 192: 522–526. [PubMed: 15695997]

36. Halbreich U Postpartum disorders: multiple interacting underlying mechanisms and risk factors. J Affect Disord 2005; 88: 1–7. [PubMed: 15996747]

37. Rubinow DR, Roy-Byrne P, Hoban MC, Gold PW, Post RM. Prospective assessment of menstrually related mood disorders. Am J Psychiatry 1984; 141: 684–686. [PubMed: 6538762]

38. Halbreich U, Endicott J. Methodological issues in studies of premenstrual changes. Psychoneuroendocrinology 1985; 10: 15–32. [PubMed: 3923510]

39. Ainscough CE. Premenstrual emotional changes: a prospective study of symptomatology in normal women. J Psychosom Res 1990; 34: 35–45. [PubMed: 2313612]

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Table 1.

Clinical and demographic characteristics in women with and without postpartum mood symptoms and bipolar disorder

Variable	Postpartum mood symptoms positive (n = 55) Mean (SD) or %	No postpartum mood symptoms (n = 248)[a] Mean (SD) or %	*t*-test (p-value) or chi-square (p-value)
Age at interview (years)	47.18 (8.93)	43.31 (10.14)	2.61 (0.009)
Age at onset (years)	19.76 (7.86)	19.29 (9.60)	0.18 (0.859)
Number of major depressive episodes	15.27 (23.61)	24.12 (50.02)	1.27 (0.202)
Number of manic episodes	20.21 (30.94)	27.96 (87.09)	0.65 (0.516)
Longest major depressive episode (weeks)	44.18 (49.42)	53.76 (88.89)	0.77 (0.440)
Number of years ill	26.11 (11.29)	24.10 (10.43)	1.27 (0.204)
Number of pregnancies	3.36 (1.82)	3.03 (1.78)	1.24 (0.216)
Number of live births	2.38 (1.47)	1.83 (1.36)	2.67 (0.008)
Years of education	14.12 (2.79)	14.21 (2.43)	0.24 (0.809)
Percent currently depressed	40.0%	45.2%	0.30 (0.584)
Marital status (% currently married)	58.2%	53.2%	0.27 (0.605)

[a]All women had a history of pregnancy.

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Table 2.

Familiality of postpartum mood symptoms in women with bipolar disorder

	Postpartum symptoms and positive family history of postpartum symptoms[a], n (%)	Postpartum symptoms and negative family history of postpartum symptoms[b], n (%)	Odds ratio[c]	p-value	95% CI
Any mood symptom	21/69 (30.43)	34/234 (14.53)	2.31	0.011	1.21–4.40
Depression only	17/58 (29.31)	29/245 (11.84)	2.71	0.005	1.35–5.47

[a]Numerator equals number of women who had postpartum symptoms and a family history of postpartum symptoms. Denominator equals total number of women with a family history of postpartum symptoms.

[b]Numerator equals number of women who had postpartum symptoms and NO family history of postpartum symptoms. Denominator equals total number of women without a family history of postpartum symptoms.

[c]All odds ratio analyses were controlled for number of live births.

CI = confidence interval.

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Table 3.

Familiality of postpartum depressive episodes in women with bipolar disorder

	PDE and positive family history of PDE[a] n (%)	PDE and negative family history of PDE[b] n (%)	Odds ratio[c]	p-value	95% CI
Within 1 month	2/14 (14.29)	8/289 (2.77)	5.79	0.038	1.100–30.39
Within 2 months	2/16 (12.50)	10/287 (3.48)	3.96	0.094	0.789–19.89
Within 3 months	2/16 (12.50)	10/287 (3.48)	3.96	0.094	0.789–19.89

[a]Numerator equals number of women who had postpartum depressive episodes and a family history of postpartum depressive episodes. Denominator equals total number of women with a family history of postpartum depressive episodes.

[b]Numerator equals number of women who had postpartum depressive episodes and NO family history of postpartum depressive episodes. Denominator equals total number of women without a family history of postpartum depressive episodes.

[c]All odds ratio analyses were controlled for number of live births.

PDE = postpartum depressive episode; CI = confidence interval.

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