Borderline personality traits are differently associated with postpartum psychosis and postpartum depression episodes in women with bipolar disorder

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Abstract

Background Women with bipolar disorder have approximately 40%-50% chance of having a perinatal bipolar recurrence. Knowing the factors associated will be beneficial for the prediction and prevention of episodes. We aim to establish if borderline personality disorder traits, as measured by the BEST (Borderline Evaluation of Severity over Time) scale, are associated with perinatal psychiatric outcomes.

Methods We recruited women with bipolar disorder as part of the BDRN (Bipolar Disorder Research Network) study. Women were interviewed and we collected their demographic and clinical information. Participants subsequently completed the BEST questionnaire. We analysed the association of BEST scores with lifetime presence/absence of perinatal bipolar relapse and, employing multinomial logistic regression, with different subtypes of perinatal outcomes: postpartum psychosis; postpartum depression, and other episodes.

Results In our sample of 807, although there was no significant association between the BEST total score and perinatal episodes as a whole (adjustedOR 1.01 CI95%[0.99, 1.03], p=0.204), we found significant differing associations with different subtypes of episodes. Women scoring highly on BEST were less likely to experience a postpartum psychotic episode (RRR 0.96 CI95%[0.94, 0.99], p=0.005) but more likely to experience a non-psychotic depressive episode (RRR 1.03 CI95%[1.01, 1.05], p=0.007) than no relapse.

Limitations This study is limited by its cross-sectional design and self-report nature of BEST.

Conclusions In women with bipolar disorder, borderline traits differentiate the risk of postpartum depression and postpartum psychosis, emphasise the importance of considering risk factors for these perinatal episodes separately, and may help individualise the risk for women in the perinatal period.

Keywords: Borderline personality traits, Bipolar Affective Disorders, Postpartum psychosis, Postpartum depression, Perinatal Psychiatry

Introduction

Perinatal episodes can have a major impact on women, their families and costs to society(Bauer et al., 2014): suicide is a leading cause of maternal death(Knight et al., 2019), illness can influence bonding with the baby and relationships can suffer(Stein et al., 2016). Therefore, being able to identify women at highest risk and working to prevent those illness episodes is a clinical, research and public health priority. Bipolar disorder affects 1-3% of the population(Merikangas et al., 2007) and for those women childbirth is a period of high risk with around of 40-50% experiencing a recurrence, which can be a manic or depressive episode, including in 20% a severe episode of postpartum psychosis(Di Florio et al., 2013; Jones et al., 2014; Wesseloo et al., 2016).

The literature suggests that co-morbid borderline personality disorder has an adverse impact on outcomes in those with bipolar disorder (e.g. suicidality and higher number of mood episodes)(Frías et al., 2016). Several factors have been studied and linked to the development of perinatal episodes in women with bipolar disorder(Jones et al., 2014) but personality disorder traits have not yet been a major focus of these studies, with only a few covering personality traits in general(Marks et al., 1992; Perry et al., 2019) and none dealing with borderline personality disorder traits specifically.

The aim of our study is to test whether borderline personality disorder traits, as assessed by the *Borderline Evaluation of Severity Over Time* (BEST) questionnaire are associated with lifetime perinatal mood episodes in women with bipolar disorder.

Methods

Sample

We recruited participants as part of a large, on-going programme of research investigating genetic and non-genetic determinants of mood disorders (Bipolar Disorder Research Network, BDRN; www.bdrn.org). We recruited participants systematically through the UK National Health Service (NHS) and non-systematically via the BDRN website, via the media (television, radio, press, social media) and patient support groups (such as Bipolar UK and Action on Postpartum Psychosis). The research programme inclusion criteria required participants to be aged 18 years or over, UK White ethnicity due to a focus on genetic aetiology, able to provide written informed consent, meet DSM-IV criteria for bipolar disorder and for mood symptoms to have started before the age of 65 years. We excluded potential participants if they had only experienced affective illness as a result of alcohol or substance misuse, or secondary to medication or another medical illness.

We included in this study participants with a lifetime DSM-IV(American Psychiatric Association, 2013) diagnosis of Bipolar disorder (type I, type II, schizoaffective bipolar and NOS) and who were parous women.

Participants were assessed by team members either at a clinic, at their house, or via telephone or videocall. The assessment included an interview where demographic, clinical and pregnancy related information was collected, the administration of questionnaires and review of case notes where available. We used the Schedules for Clinical Assessment in Neuropsychiatry (SCAN)(Wing et al., 1990), a semi-structured interview which was administered by trained research psychiatrists or psychologists to assess clinical outcomes.

We made best-estimate main lifetime diagnosis according to DSM-IV(American Psychiatric Association, 2013) criteria and rated key clinical variables, such as age at onset of impairment and number of admissions. In cases of ambiguity, at least two members of the research team made the clinical and diagnostic ratings blinded to each other and consensus was agreed through discussion. For inter-rater reliability, mean kappa statistics were 0.85 for DSM–IV diagnosis, 0.97 for perinatal mood episodes and between 0.81 and 0.99 for other key clinical categorical variables. Mean intra-class correlation coefficients were between 0.91 and 0.97 for key clinical continuous variables.(Perry et al., 2016)

Measuring borderline personality disorder traits

We measured borderline personality disorder traits using *The Borderline Evaluation of Severity Over Time* (BEST) scale(Blum et al., 2002; Pfohl et al., 2009), which was sent to participants as a mail-out in 2013 as follow-up questionnaire. Participants were asked to rate the items thinking about the course of their life in general (i.e. not specifically about episodes of mood illness). The BEST scale is a 15-item self-rated questionnaire to assesses borderline personality disorder traits. It was originally developed to allow patients on a cognitive-behavioural systems-based group treatment to rate the degree of impairment from each of the nine borderline personality disorder criteria over the previous week.(Blum et al., 2002) Each item is rated in a scale from 1 to 5 (lowest to highest rating of severity). It originally consisted of 3 subscales (A, B and C) with each item rated in a five-point scale. Subscale C was about positive behaviours related to that treatment program and not relevant to our study. Therefore, in our study we used subscale A which measures thoughts and feelings (8 items, range 8-40) and subscale B which measures negative behaviours (4 items, range 4-20) and the total scores of the version we used ranged from 12 to 60. We

used the BEST to measure the severity of such symptoms over lifetime, making an assumption on the temporal stability (trait rather than state) of the BEST and did not use cut offs as we were interested in the impact of traits on perinatal outcomes across the range of symptoms experienced rather than merely in those with a formal co-morbid diagnosis. At the time the BEST questionnaire was completed, participants' current mood state was also measured using the Beck Depression Inventory (BDI) (Beck et al., 1961) and the Altman Mania Scale (AMS)(Altman et al., 1997).

Co-variates

We selected potential confounders based on the literature and agreed with the research team: age at interview, age at onset of impairment of bipolar disorder, number of admissions, family history of postnatal mental illness, number of pregnancies, diagnosis subtype (bipolar type I, type II, schizoaffective bipolar and NOS) and current mood measured by the BDI (Beck et al., 1961) and AMS (Altman et al., 1997) scales).

Lifetime perinatal psychiatric outcomes

Our outcomes of interest were lifetime perinatal psychiatric outcomes. They were assessed during the interview and complemented by information from case notes where available. Mood and psychotic symptomatology of perinatal episodes was assessed using the SCAN. We were interested in the most severe postpartum episode experienced and took a lifetime approach: for each participant the most severe perinatal psychiatric episode was rated as the lifetime most impairing perinatal episode and considered as outcome i.e. if one participant had a postpartum psychotic episode in one pregnancy and a postpartum non-psychotic depressive episode in another pregnancy, the psychotic episode was rated.

Women were grouped according to lifetime occurrence of perinatal psychiatric outcomes: 0 = no relapse despite giving birth; 1 = Postpartum Psychosis (PPP) defined as postpartum mania / psychotic episode, which includes all psychotic and/or manic episodes occurring within 6 weeks of giving birth (PPP); 2 = postpartum non-psychotic depressive episode (PNPD) occurring within 6 weeks of giving birth; 3 = other perinatal episodes, which include those which do not meet criteria for categories mentioned above, such as hypomania or mood episode with onset during pregnancy or beyond six weeks (see Supplement Figure 1 and Table 1).

We chose these categories based on the severity of episodes, and consistent with the approach we took in other studies(Di Florio et al., 2013). We were interested in episodes with onset within 6 weeks of childbirth as these are more likely to be triggered by childbirth and to be consistent with both ICD (within 6 weeks) and DSM (within 4 weeks) temporal definitions of the postpartum period.

Analysis

The data was analysed using Stata IC version 16 for Mac OS.

We tested the association between BEST scores and perinatal psychiatric outcomes in two main ways using logistic regression. Firstly, we tested the association between BEST scores and presence of perinatal relapse using binary logistic regression (relapse vs no relapse). We then conducted multinomial logistic regression analysis with the four perinatal psychiatric outcomes as outcome variable (PPP vs PNPD vs other perinatal episodes vs no relapse), and the BEST scores as main exposure variable.

BEST scores were calculated by adding the scores of each individual item and were used in the analysis as a continuous variable. In addition to the BEST total scores, we considered the two subscales of BEST (total score of each subscale) and scores (scale of 1 to 5) of some individual questions. As there is some overlap in the symptoms of borderline and bipolar disorders we conducted further analysis at the level of individual BEST items focusing only on those that represent symptoms of borderline personality disorder but not bipolar disorder: fear of abandonment, major shifts in opinion of others, feelings of emptiness and 'going to extremes to keep someone from leaving you' (items 1,2,7 and 9).

We conducted a sensitivity analysis, splitting total BEST scores into quintiles (Supplement Figure 2) to explore the relationship and assist interpretation. We performed further sensitivity analysis including only those with bipolar subtype I as they are the ones likely to experience postpartum psychosis.(Di Florio et al., 2013)

Multinomial regression is an extension of logistic regression that is used when a categorical outcome variable has more than two values and predictor variables are continuous or categorical. Therefore, we used multinomial regression to predict which of the possible perinatal psychiatric outcomes a woman is likely to belong to, compared to a reference category (no relapse) and given certain other information (co-variates). We performed multinomial logistic regression, unadjusted (not presented) and then adjusting for the pre-specified potential confounders. We present the results as Relative Risk Ratios (RRR) for ease of interpretation. We did the standard model fitting checks to test for collinearity between the predicting variables and were able to include all pre-specified variables except BDI as it was significantly and highly correlated (0.6) with BEST total scores.

A complete case-analysis approach was employed for all analyses.

Ethical approval

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. All procedures involving human participants had NHS Health Research Authority (HRA) approval – Research Ethics Committee (REC) reference ((MREC/97/7/01) and local approvals in all participating NHS Trusts/Health Boards. Written informed consent was obtained from all participants.

Results

Sample

Eight hundred and seven women who met the inclusion criteria for the BDRN study, were parous and had completed the BEST questionnaire were included in the analysis (see Supplement flowchart Figure 1).

The mean age at interview was 50.3 years and the median number of pregnancies was 2. The majority (66.0%) had a diagnosis of bipolar disorder type I (Table 1), because BDRN recruitment focused on more severe forms of bipolar disorder.

[Table 1 here]

Association between BEST scores and overall perinatal recurrence

We first looked at whether BEST scores were associated with the lifetime presence of perinatal recurrence in our sample, employing binary logistic regression and adjusting for the cofounders mentioned above. There was no significant association between the BEST

total score and presence of any perinatal episodes (aOR 1.01 CI95% [0.99, 1.03], p= 0.204). A sensitivity analysis with total BEST scores split in quintiles did not change the results. There was also no significant association between the score of BEST subscale A (aOR 1.05 CI95% [0.99, 1.04], p= 0.230) or subscale B (aOR 1.03 CI95% [0.98, 1.09], p= 0.214) with overall perinatal recurrence.

Association between BEST scores and subtypes of perinatal psychiatric outcomes

Although we found no association between postpartum episodes as a whole and BEST scores, we then looked at the relationship of BEST scores with the different subtypes of perinatal psychiatric outcome groups (postpartum psychosis, postpartum depression and other perinatal episodes). We found that after controlling for potential confounders, women who had higher BEST total scores were significantly less likely to have a postpartum psychotic episode (RRR 0.96 CI 95%[0.94, 0.99] p=0.005) and significantly more likely to have a non-psychotic depressive episode within 6 weeks of childbirth (RRR 1.03 CI 95% [1.01, 1.05] p=0.007) or to have other perinatal episode (RRR 1.03 CI 95% [1.00, 1.05] p=0.021) than no relapse. Table 2 and Figure 1 show the Relative Risk Ratio (RRR), estimating the probability of women having any relapse relative to 'no relapse' (the most common perinatal psychiatric outcome), derived from the fully adjusted multinomial logistic regression model. For BEST subscale A (thoughts and feelings) and subscale B (negative behaviours), we observed exactly the same pattern of associations and same significant associations as BEST total score (See Table 2).

[Figure 1 here]

[Table 2 here]

In particular, those who scored on the highest quintile of BEST compared with those who scored on the lowest quintile had a significantly lower risk of PPP than no relapse (RRR 0.33 CI 95% [0.12, 0.90, p=0.031], see Supplement Table 2. On the other hand, for those who never developed postpartum psychosis, but instead developed an episode of non-psychotic postpartum depression, the highest their BEST total score the more likely to develop postpartum depression. For those in the highest BEST quintile their RRR was 2.62 higher (CI 95% [1.13, 6.09] p=0.025) than those on the lowest quintile, see Supplement Table 2.

Restricting analysis to those with a diagnosis of bipolar I does not change the findings of associations with BEST total scores. The same associations between BEST total scores and perinatal psychiatric outcomes are significant in all groups (see Supplement Table 3).

Figure 2 shows the predicted probabilities of the outcomes PPP and PNPD given BEST scores at intervals of 10. PPP probability decreases with increasing BEST scores whilst PNPD increases.

[Figure 2 here]

A further sensitivity analysis where 'other perinatal episodes' were considered together with no relapse showed the same pattern of association: those who had higher BEST total scores were significantly less likely to have a postpartum psychotic episode RRR 0.95 (CI 95% [0.93, 0.97] p=0.001) and more likely to have a PNPD RRR 1.02 (CI 95% [1.00, 1.03] p=0.083) compared to no relapse, although the latter is not significant. If we exclude people

with those 'other perinatal episodes' from the analysis the same pattern of association remains, both significantly – RRR 0.97 (CI 95% [0.94, 0.99] p=0.010) for PPP and RRR 1.03 (CI 95% [1.01, 1.05] p=0.006) for PNPD.

Analysis of individual traits measured by BEST

We found the same pattern of results of the main analysis. All these traits were negatively associated with PPP and positively associated with PNPD, with the majority p=<0.05 (See table 2).

Discussion

This is the first time, to our knowledge that borderline personality disorder traits have been assessed in women with a diagnosis of bipolar disorder and in relation to psychiatric outcomes following childbirth.

We found that there was no significant association between BEST scores and having a perinatal recurrence when all perinatal episodes were considered together. Interestingly, however, when we distinguished between different types of perinatal psychiatric episodes, namely postpartum psychosis and postpartum depression, we were able to find significant and relevant associations in opposite directions. Women with higher BEST scores were significantly less likely to have experienced an episode of postpartum psychosis (RRR 0.96 CI95% [0.94, 0.99], p=0.005) but significantly more likely to have experienced an episode of non-psychotic postpartum depression (RRR 1.03 CI95% [1.01, 1.05] p=0.007) than no relapse.

Possible explanations for these findings

Given the overlap in symptoms between bipolar disorder and borderline personality disorder and the difficulty often in distinguishing clinically between these diagnoses(Zimmerman and Morgan, 2013), one explanation of our results could be that those with the highest BEST scores are misdiagnosed as bipolar disorder and should more appropriately be labelled under the personality disorder rubric(Saunders et al., 2015). As not representing 'true' bipolar disorder, they may therefore be less likely to develop PPP. We are confident however, that all participants meet diagnostic criteria for bipolar disorder, as the diagnostic process was robust including a detailed SCAN interview and case note review. There can be however co-morbidity between the two. The interview for this cohort, which is a cohort of people with a diagnosis of bipolar disorder, does not formally assess for a diagnosis of borderline personality disorder and therefore we don't know how many also had a diagnosis of borderline personality disorder. That our findings are not merely the result of misdiagnosis or co-morbidity is supported by another two lines of evidence. First, although co-morbidity and diagnostic overlap with borderline personality disorder are more of an issue in bipolar II than bipolar I, with approximately 10% of bipolar I and 20% of bipolar II patients also diagnosed with borderline personality disorder(Zimmerman and Morgan, 2013), we find exactly the same pattern of results when limiting the analyses to women with bipolar I. Therefore it cannot be explained by the high co-morbidity of bipolar II.

Second, the findings are not driven solely by very high scores that would represent those women with a potential categorical diagnosis of borderline personality disorder, but rather

there is a relationship with perinatal outcomes across the spectrum of BEST score as shown by the predicted probabilities analysis.

Further support for the validity of the relationship between borderline traits and perinatal episodes comes from the analysis focussing on symptoms which are particularly characteristic of borderline personality disorder and do not overlap with those of mood disorders. These symptoms include fear of abandonment, major shifts in opinion of others, feelings of emptiness and going to extremes to keep someone from leaving you. We found these individual symptoms were associated with higher risk of non-psychotic postpartum episodes of depression and with lower risk of PPP.

Implications

Our findings have implications for the study of perinatal episodes and add to the data supporting the need to stratify perinatal episodes by type.(Florio et al., 2018) No association was found for perinatal episodes when taken as a whole but interesting differences emerged when postpartum psychosis was differentiated from postpartum depression. Studies examining risk of perinatal episodes in bipolar women must therefore differentiate between these individual outcomes.

Our results may also help us understand potential different aetiologies of perinatal episodes with personality factors playing a role in increasing risk of non-psychotic postpartum depression but a reduced risk of a postpartum psychotic episode. Episodes of postpartum psychosis occurred in a more homogeneous bipolar group i.e. women with a bipolar

diagnosis with low levels of borderline specific symptoms. This adds to evidence from our previous study which demonstrated that personality traits usually associated with bipolar disorder, such as higher levels of neuroticism, impulsivity and schizotypy, were not associated with risk of severe postpartum episodes, over and above their impact on the underlying mood disorder(Perry et al., 2019). An older study(Marks et al., 1992) with a small sample found that higher levels of neuroticism were associated with non-psychotic postpartum mood episodes, but not psychosis, among women with a history of mood disorders (n=26 with bipolar disorder or schizoaffective disorder) and in those with no such history. The reasons for the associations found remain unexplained and further work is needed to understand those.

Finally, the findings are relevant clinically to support discussion about risk with women and their families. Considering personality traits dimensionally appears to be more helpful than a simple categorical diagnosis of personality disorder and can help individualise the risk of perinatal recurrence. In addition, many women with a label of borderline personality disorder have a history of developmental trauma and may be better conceptualised as complex Post Traumatic Stress Disorder (PTSD)(Watts, 2019). It is possible that the link between borderline traits and non-psychotic postpartum episodes may be related to the anticipation of childbirth reactivating childhood traumas.(Zanarini and Frankenburg, 1997) Our results therefore, act as a reminder of considering screening women for history of trauma in the assessment of perinatal risk in bipolar women.

Limitations

This study is limited by its cross-sectional design. However, the questionnaire is designed to measure personality traits, which should be constant throughout one's life and we adjusted for their age at interview. It is also possible some women became pregnant and had further postpartum episodes after our interview, which could change their outcome category if they had a PPP. However, at the time of interview the majority of women were already passed their reproductive years and we included age at interview, number of pregnancies and measures of severity as confounders in the analysis. The cross-sectional and retrospective design also means that some information may not be reliable, such as the use of medication which we were not able to take into consideration in this analysis. This is also a highly educated sample that may not be representative of the general population.

Another limitation is that the BEST scale is self-report and was not designed to address borderline traits in people specifically with bipolar disorder and the questionnaire asks about overlapping symptoms. Therefore, our interpretation should be based on the content of the scale i.e. presence and severity of borderline personality disorder symptoms and this is also why we performed further analysis on non-overlapping symptoms as discussed above. Although the BEST may not be ideal, in this study we have asked participants to consider the symptoms over their lifetime, therefore assessing borderline personality disorder traits rather than symptoms limited to a restricted period. The scale has now already been successfully employed in the bipolar population(Saunders et al., 2020) which reassures us of its applicability. This is a cohort of women with bipolar disorder and we do not have information about the onset of symptoms of borderline personality disorder. Further work might address this limitation.

In summary, this study adds to other evidence from our cohort that suggest different risk factors are associated with PPP and PNPD in bipolar women.(Perry et al., 2020, 2016) Knowing that someone has borderline personality disorder traits might help identify those who are less likely to develop postpartum psychosis and more likely to have a non-psychotic depressive episode, helping to individualise a women's risk of relapse. It also has implications for research into perinatal episodes and stresses the need to stratify analysis of perinatal recurrence by type of episode.

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Table 1. Clinical and demographic information at the time of interview (total sample n=807) and distribution of BEST scores

	Mean/Median*	**s.d./IQR***	**Min**	**Max**
Age at interview/years (n=807)	50.3	10.8	21	80
Number of pregnancies* (n=775)	2	1-10	1	15
Age of onset of impairment*/years (n=770)	21	7-55	6	60
Number of admissions* (n=786)	2	0-24	0	35
BDI (n=793)	15.3	12.2	0	59
AMS* (n=802)	3	0-16	0	20
Highest Education ** (n=766)				
Higher				316 (41.2%)
No-higher				450 (58.8%)
Highest Occupation** (n=764)				
Professional				394 (51.6%)
Non-professional				360 (47.1%)
Never worked				10 (1.3%)
Type of recruitment** (n=785)				
Systematic				216 (27.5%)
Non-systematic				569 (72.5%)
Ever married or lived as married** (n=787)				
No				25 (3.2%)
Yes				762 (96.8%)

DSM Diagnosis** (n=807) BP type I BP type II SA BP BP NOS				533 (66.1%) 230 (28.5%) 18 (2.2%) 26 (3.2%)
Family history of postnatal psychiatry episodes ** (n=608) No Yes				534 (87.8%) 74 (12.2%)
BEST total score	31.0	12.9	12	60
BEST subscale A	21.9	9.0	8	40
BEST subscale B	9.1	4.4	4	20

s.d., standard deviation; IQR, Interquartile range; BDI, Beck Depression Inventory; AMS, Altman Mania Scale

**Medians and upper/lower quartiles presented instead of means and s.d. because of skewed data*

***n, %*

Table 2. Fully adjusted relative risk ratio estimates (RRR) from multinomial logistic regression models for associations of BEST total score, BEST subscales, and BEST questions 1, 2, 7 and 9 with perinatal psychiatric relapse (against no relapse as the referent group) (N=555).

	Type of relapse	**RRR** (compared to no relapse)	**S.E.**	**P-value**	**[95% Conf. Interval]**	
BEST total	**PPP**	0.963	0.013	0.005*	0.939	0.989
	PNPD	1.030	0.011	0.007*	1.008	1.052
	other	1.026	0.011	0.021*	1.004	1.048
BEST subscale A (Thoughts and Feelings)	**PPP**	0.952	0.017	0.007*	0.919	0.987
	PNPD	1.042	0.016	0.008*	1.010	1.074
	other	1.036	0.016	0.025*	1.004	1.068
BEST subscale B (Negative Behaviours)	**PPP**	0.908	0.035	0.012*	0.842	0.979
	PNPD	1.079	0.033	0.013*	1.016	1.146
	other	1.069	0.033	0.033*	1.005	1.136
Q1 – Fear of abandonment	**PPP**	0.772	0.079	0.012*	0.632	0.944
	PNPD	1.101	0.095	0.267	0.929	1.305
	other	1.121	0.099	0.196	0.943	1.333
Q2 – Major shifts in opinion about others	**PPP**	0.777	0.082	0.017*	0.632	0.956
	PNPD	1.295	0.118	0.005*	1.083	1.549
	other	1.158	0.107	0.113	0.966	1.387
Q7 – Feelings of emptiness	**PPP**	0.824	0.083	0.055	0.677	1.004
	PNPD	1.202	0.113	0.050	0.999	1.445

	other	1.229	0.117	0.030*	1.020	1.481
Q9 – going to extremes to keep someone from leaving you	**PPP**	0.838	0.106	0.162	0.654	1.074
	PNPD	1.108	0.111	0.304	0.911	1.349
	other	1.170	0.118	0.118	0.961	1.426

Adjusted for age at interview, age at onset of impairment of bipolar disorder, number of admissions, family history of postnatal mental illness, number of pregnancies, diagnosis subtype (bipolar type I, type II, schizoaffective bipolar and NOS) and current mood (AMS scale).