Distinct Genetic Profiles in Postpartum Depression With Different Trajectory of Illness

Nagahide Takahashi (✉ n-taka@hama-med.ac.jp)  
Hamamatsu Ika Daigaku  
https://orcid.org/0000-0002-7711-0297

Hanae Tainaka  
Hamamatsu Ika Daigaku

Tomoko Nishimura  
Hamamatsu Ika Daigaku

Taeko Harada  
Hamamatsu Ika Daigaku

Akemi Okumura  
Hamamatsu Ika Daigaku

Damee Choi  
Hamamatsu Ika Daigaku

Toshiki Iwabuchi  
Hamamatsu Ika Daigaku

Hitoshi Kuwabara  
Hamamatsu Ika Daigaku

Shu Takagai  
Hamamatsu Ika Daigaku

Yoko Nomura  
Queens College

Nori Takei  
Hamamatsu Ika Daigaku

Kenji. J Tsuchiya  
Hamamatsu Ika Daigaku

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Abstract

Background
Postpartum depression (PPD) is a common and highly heritable disorder in the postnatal period of new mothers. The development of PPD is shown to affect neurodevelopment in children and recent evidence suggests that the trajectory of PPD is also associated with children's neurodevelopment and mental conditions. Thus, early identification and intervention for individuals at high risk of PPD are urgently needed. Additionally, it is not clear whether genetic factors affect the trajectory of PPD. Therefore, using a polygenic risk score (PRS) approach, we investigated if PRS for depression (Depression-PRS) and bipolar disorder (Bipolar-PRS) are associated with the development and clinical course of PPD.

Methods
Using recent large genome-wide association studies (GWAS) of depression and bipolar disorder as discovery cohorts, we calculated Depression-PRS and Bipolar-PRS in each individual. Then, we investigated the possible association between Depression-PRS and Bipolar-PRS with the development and trajectory of PPD in subjects from the Hamamatsu Birth Cohort for mothers and children (n = 136). Depressive symptoms were assessed using the Edinburgh Postpartum Depression Scale. Gene-set enrichment analyses were used to identify pathways underlying these conditions.

Results
Depression-PRS was significantly higher in subjects with PPD than in those without PPD (t = -3.283, P = 0.002) and logistic analysis showed that Depression-PRS significantly increases the risk of developing PPD (OR [SE] = 2.274 [0.585], P = 0.002). Furthermore, Depression-PRS was positively associated with continuity of PPD (β [SE] = 1.621 [0.672]; P = 0.032). Gene-set enrichment analyses revealed that pathways such as “response to hormone” (β [SE] = -2.285 [1.002], P < 0.001) and “epigenetic regulation” (β [SE] = 2.831 [1.317], P < 0.001) were involved in the continuity of PPD.

Conclusion
These preliminary findings indicate that the genetic component plays an important role not only in the development but also in the continuity of PPD. A polygenic risk score approach could be useful to identify subjects at risk for PPD, especially for persistent PPD, who need careful monitoring and intervention after delivery.

Background
Postpartum depression (PPD) is a common psychiatric disease observed among new mothers in the postnatal period, with a reported prevalence higher than 20% [1]. Recent studies, including our own, suggest that PPD affects children's neurodevelopment and their subsequent mental health [2–6]. Additionally, the trajectory of PPD has been reportedly associated with these children's behavioral outcomes [6–8]. Thus, early identification and intervention for individuals with high risk for PPD are urgently needed.

In the American Psychiatric Association's Diagnostic and Statistical Manual of Disorders, fifth edition [9], PPD is defined as a major depressive episode with onset during pregnancy or in the 4 weeks following delivery. However, many studies have defined PPD as a depressive episode that occurs from 4 weeks to 12 months after childbirth [10]. While it is well known that PPD follows different trajectories among
individuals, little research has been conducted to examine the factors influencing these variabilities among different individuals [1].

Meanwhile, evidence suggests that genetic factors play an important role in the development of PPD [11, 12]. Indeed, the heritability of PPD is estimated to be as high as 50% [13], which is much higher than that of major depressive disorder. More recently, other factors such as a past history of depression, social conditions, and hormonal levels have been discussed as possible factors that may influence the individual differences related to the trajectory of PPD [14]. Little is known, however, about whether genetic factors are involved in the trajectory of PPD.

In this pilot study, we attempted to investigate whether genetic factors were associated with the trajectory of PPD using a polygenic risk score (PRS) approach capitalizing on the data of a part of our birth cohort study, the Hamamatsu Birth Cohort for Mothers and Children (HBC study). Notably, since recent systematic reviews have reported that some subjects with a high Edinburgh Postpartum Depression Scale (EPDS) score were later diagnosed as having a bipolar disorder [15, 16], we used PRS for both the unipolar and bipolar disorders in our analysis.

**Methods**

**Participants**

Participants in this study (n = 136) were mothers who gave birth to their children in Japan between December 2007 and June 2011 with DNA genotyping data from an HBC study (total participants = 1138). Recruitment procedures are comprehensively described in our previous studies [17]. The study procedures were approved by the Hamamatsu University School of Medicine and University Hospital Ethics Committee (research ID: 17–037 and 19–145) and written informed consent was obtained from each mother for the participation of her infant in our study. This study followed the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) reporting guidelines.

**Measurement**

Depressive symptoms were assessed by using the Japanese version of Edinburgh Postpartum Depression Scale (EPDS) at week 1 and 4, 3 months, and 10 months after delivery. The cut-off score for EPDS was 9, which is widely used and validated in the PPD study for Japanese subjects [18]. Mothers whose EPDS score was above the cut-off point within 3 months or 10 months postpartum were defined as subjects with “PPD at any time point”.

Mothers whose EPDS score was above cut-off point only within 3 months postpartum were defined as subjects with “transient PPD.” Mothers whose EPDS score was above the cut-off point at both within 3 months and at 10 months postpartum were defined as subjects with “persistent PPD”. Since it is difficult to identify the exact date of onset among mothers whose EPDS score was above the cut-off point only at 10 months postpartum, these mothers were assigned to subjects with “persistent PPD” in the analyses.
Genotyping, Quality Control, and Imputation

Genotyping was conducted using the Japonica array, designed for single nucleotide polymorphism (SNP) genotyping specific for the Japanese population [19]. Briefly, the quality controls retaining SNPs and subjects were as follows: missing data for SNP $< 0.02$, pairwise Identify-By-Descent (IBD) $< 0.2$, SNP Hardy Weinberg equilibrium of $p > 10^{-6}$, and minor allele frequency $> 0.01$. No individual was removed from the analysis as “related subjects” in an identity-by-descent analysis. Genotyping imputation was performed using BEAGLE 4.1 [20] with Phase 3 of the 1000 Genome Project as a reference panel for the Japanese population (https://www.internationalgenome.org). SNPs with an imputation INFO score $< 0.8$ were excluded. We also excluded SNPs located within the MHC region because of high linkage disequilibrium (LD) in this region. The number of SNPs analyzed was 5,606,655.

PRS analysis

We used PRSice-2 to generate PRS, according to the developers’ protocol [21]. The summary GWAS data used to determine the PRS for depression (Depression-PRS) and bipolar disorder (Bipolar-PRS) were obtained from the Psychiatric Genomics Consortium (https://humandbs.biosciencedbc.jp/en/). To account for population stratification, we included 4 principle components (PCs). The PCs were calculated based on the pruned data with PLINK 1.9 [22]. The criteria for SNP clumping was pairwise LD $r^2 < 0.1$ within 1 Mb window. PRS scores were calculated with P value thresholds at 0.05, which is widely accepted [23]. The number of SNPs used for calculating Depression-PRS and Bipolar-PRS were 126,868 and 290,127, respectively. Standardized PRS scores (mean = 0 and standard deviation = 1) were used for the analyses.

Gene-set analyses were conducted using PRSet function implemented in PRSice-2. The collection of gene-sets was obtained from the MSigDB database and GO gene sets (c5:Biological Process) were used for the analyses (http://software.broadinstitute.org/gsea/msigdb/index.jsp).

Statistical analysis

Demographic differences between subjects without PPD, with “transient PPD,” and “persistent PPD” were tested, using the analysis of variance for continuous variables, and the chi-square test for categorical variables. Paired t-test was used for comparing Depression-PRS and Bipolar-PRS between subjects without PPD and subjects with “PPD at any time point.” P-value was corrected by Bonferroni corrections for multiple testing (2 independent hypotheses: Depression-PRS and Bipolar-PRS) and the significance of P-value was set at 0.05.

The associations of PPD trajectory with Depression-PRS and Bipolar-PRS were analyzed using multinomial logistic regression analysis. Age at childbirth, household incomes, emotional support, maternal educational attainment (in years), and maternal pre-pregnancy body mass index (BMI) were included as covariates. Again, P-value was corrected by Bonferroni corrections for multiple testing (2 independent hypotheses: Depression-PRS and Bipolar-PRS) and the significance of P-value was set at 0.05.
For gene-set enrichment analysis, P value was corrected using 10000 permutation tests and the significance was set at 0.05. All statistical analysis was two-tailed and was conducted by Stata version 15.

Results

Participant characteristics

A summary of participant characteristics is provided in Table 1. A total of 136 participants were analyzed and 25 subjects developed PPD after delivery (18.4%). Twenty subjects (14.7%) developed “transient PPD” and 5 subjects (3.7%) developed “persistent PPD”. There was no difference in the participant characteristics among groups.

![Table 1](image)

**Depression-PRS, Bipolar-PRS, and development of PPD**
Depression-PRS was significantly higher in subjects assigned to “PPD at any time point” group compared to subjects without PPD (t = -3.283, df = 134, P = 0.0026) (Fig. 1a, Table 2). On the contrary, there was no difference in Bipolar-PRS between these two groups (Fig. 1b, Table 2). Logistic regression analysis including age, household incomes, emotional support, maternal educational attainment, and BMI as covariates showed that Depression-PRS was the only factor increasing the risk of PPD (Odds Ratio [SE] = 2.272 [0.606], P = 0.002).

Table 2
Depression-PRS and Bipolar-PRS between subjects with or without PPD.

| Group                        | Depression-PRS | Bipolar-PRS |
|------------------------------|----------------|-------------|
|                              | Mean  | SE   | t     | P-value | Mean  | SE   | t     | P-value |
| No PPD (N = 111)             | -0.131| 0.915| -3.283| **0.0026| -0.017| 0.094| -0.713| 0.477   |
| PPD at any time point (N = 25)|  0.576| 0.202|       |         |  0.140| 0.209|       |         |

Abbreviations: PRS, polygenic risk score; PPD, postpartum depression; SE, standard error

** P-value < 0.01 after Bonferroni correction.

Depression-PRS, Bipolar-PRS, and trajectory of PPD

Next, we examined if Depression-PRS and Bipolar-PRS are associated with PPD trajectory using multinomial logistic regression analysis. Depression-PRS was significantly associated with “transient PPD” (β [SE] = 0.636 [0.281], P = 0.048) and “persistent PPD” (β [SE] = 1.621 [0.672], P = 0.032) (Fig. 2a, Table 3). However, Bipolar-PRS was not associated with PPD trajectory (Fig. 2b, Table 3).
Table 3
Association of PPD trajectory with Depression-PRS and Bipolar-PRS.

| Group                  | Depression-PRS | Bipolar-PRS |
|------------------------|----------------|-------------|
|                        | β     | SE   | P-value | β     | SE   | P-value |
| No PPD (N = 111)       | [Reference] | –    | –       | [Reference] | –    | –       |
| Transient PPD (N = 20) | 0.636 | 0.281 | 0.048   | 0.300 | 0.261 | 0.250   |
| Persistent PPD (N = 5) | 1.621 | 0.672 | 0.032   | -0.545 | 0.497 | 0.273   |

Abbreviations: PPD, postpartum depression; PRS, polygenic risk score; SE, standard error; NA, not applicable

P-values are corrected for Bonferroni multiple comparisons.

Gene-set enrichment analysis of PPD trajectory

To obtain biological insights related to PPD trajectory, we conducted a gene-set enrichment analysis between the “transient PPD” and “persistent PPD” groups. Table 4 shows the top 10 gene ontologies involved in PPD trajectory. Of note, “GO:0048545, response to hormone” (β [SE] = -2.285 [1.002], P < 0.001) and “GO: 0070933, histone H4 deacetylation” (β [SE] = 2.831 [1.317], P < 0.001) were identified as modulators for PPD trajectories.
Table 4  
Top 10 Gene Sets enriched in the persistence of PPD.

| Gene-set                                      | P-value threshold | $R^2$  | $\beta$  | SE    | Number of SNPs | P-value |
|-----------------------------------------------|-------------------|--------|----------|-------|----------------|---------|
| positive regulation of smooth muscle cell migration | 0.123             | 0.430  | 1.497    | 0.650 | 33             | 0.0001  |
| negative regulation of axon guidance         | 0.206             | 0.597  | 1.841    | 0.812 | 42             | 0.0003  |
| response to tumor cell                       | 0.245             | 0.408  | 1.098    | 0.494 | 25             | 0.0003  |
| response to hormone                          | 0.034             | 0.497  | -2.285   | 1.002 | 190            | 0.0004  |
| embryonic skeletal system development         | 0.342             | 0.402  | 0.704    | 0.328 | 134            | 0.0005  |
| histone h4 deacetylation                      | 0.229             | 0.416  | 2.831    | 1.317 | 10             | 0.0005  |
| protein localization to nucleus               | 0.107             | 0.441  | 1.074    | 0.505 | 61             | 0.0006  |
| hindbrain development                         | 0.441             | 0.399  | -2.987   | 1.366 | 187            | 0.0008  |

Abbreviations: PPD = postpartum depression; PRS = polygenic risk score; SE = standard error; SNP = single nucleotide polymorphism.

**P-value < 0.01**

Abbreviations: PPD, postpartum depression; PRS, polygenic risk score; N.S, not significant.

*P-value < 0.05, **P-Value < 0.01
| Gene-set                                      | P-value threshold | $R^2$  | $\beta$   | SE    | Number of SNPs | P-value |
|----------------------------------------------|-------------------|--------|-----------|-------|---------------|---------|
| positive regulation of cellular component organization | 0.366             | 0.501  | -3.895    | 1.867 | 1070          | 0.0008  |
| localization within membrane                 | 0.309             | 0.478  | -1.352    | 0.646 | 215           | 0.0010  |

Abbreviations: PPD = postpartum depression; PRS = polygenic risk score; SE = standard error; SNP = single nucleotide polymorphism

Abbreviations: PPD = postpartum depression; PRS = polygenic risk score; N.S = not significant.

**P-value < 0.01**

Abbreviations: PPD, postpartum depression; PRS, polygenic risk score; N.S, not significant.

*P-value < 0.05, **P-Value < 0.01

**Discussion**

In the present study, first, we confirmed that the genetic risks of major depression, as measured using the PRS, are associated with the development of PPD in our cohort study. Next, we found that the genetic risk of major depression affects the trajectory of PPD.

Using PRS analysis, we found that Depression-PRS was significantly higher in subjects with “PPD at any time point” than in subjects without PPD. Furthermore, Depression-PRS was higher in subjects with “persistent PPD” than in subjects with “transient PPD.” To our knowledge, this is the first study demonstrating that genetic factors are involved in the development and trajectory of PPD using the PRS approach.

The prevalence of PPD in the current study was 18%, which is similar to the results of previous studies [1, 24]. Moreover, approximately 20% of mothers who developed PPD showed persistent symptoms 10 months postpartum, supporting the notion that there are strong individual differences in PPD trajectories [25]. The present results suggest that there might be biological differences between transient PPD and persistent PPD. Lapato et al. [26] reported that women who experienced their first symptoms of major depression in the peripartum have different genetic backgrounds, as compared to those who have recurrent major depression and happen to develop symptoms during the peripartum. In our gene-set analyses, we found that genes associated with hormone response and epigenetic changes were involved in the persistence of PPD. In conjunction with our current results, several studies have shown that reproductive hormones, such as lactogenic hormones and thyroid function, were related to the development of PPD [14, 27]. More recently, it has been proposed that hormones such as glucocorticoid...
cause treatment-resistant depression through epigenetic changes in the brain [28]. It is possible that different courses of PPD are due to different severities of the illness between transient and persistent PPD groups. However, there was no difference in the mean EPDS scores between subjects with “transient PPD” and “persistent PPD” (t = -1.510, df = 18, P = 0.148). Taken together, we can safely conclude that the trajectory of PPD is mainly affected by genetic factors.

In the current study, contradictory to the prior study by Munk et al. [26], which reported that the diagnosis of women with initial diagnosis of major depression was more likely to change to bipolar disorder in 15 years of follow-up periods, in our study, Bipolar-PRS was not associated with the development of PPD [16]. While these findings were inconsistent with ours, the differences may be explained by the variations in our subject characteristics. That is, while all subjects in the study by Munk et al. were clinical patients, and were referred to psychiatric hospitals, our participants were drawn from a general population.

There are a few limitations that should be considered in our study. First, the sample size was relatively small; thus, we had only 25 subjects with PPD in the analysis. Second, we did not have information about whether our participants with depressive symptoms had taken their medication and received psychological treatment for PPD. Third, our cases with PPD were ascertained using a screening tool, the EPDS, and not via a clinical interview conducted by a research clinician. Future studies using a larger sample size with PPD assessed via a structured clinical interview for the DSM and replications in different cohorts are needed.

Conclusions

In this pilot study, using a part of data from a longitudinal cohort study, we demonstrated that genetic factors for depression are associated with the development and trajectory of PPD. Our study provided initial evidence that a polygenic risk score approach could be used for early identification of individuals with a high risk for PPD and for a prediction of the trajectory of PPD. We hope that these initial findings will eventually lead to effective interventions for PPD.

List Of Abbreviations

PPD, postpartum depression; PRS, polygenic risk score; EPDS, Edinburgh Postpartum Depression Scale; GO, Gene Ontology

Declarations

Ethics approval and consent to participate:

The study procedures were approved by the Hamamatsu University School of Medicine and the University Hospital Ethics Committee (research ID:17–037 and 19–145) and written informed consent was obtained from all participants.
Consent for publication:

Not applicable.

Availability of data and materials:

All the data supporting our findings are contained within the manuscript. Therefore, data sets are not shown.

Competing interests:

None

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Authors' contributions:

Dr. Takahashi had full access to all the data used in the study and takes responsibility for the integrity of the data and accuracy of the data analysis.

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References

1. Howard LM, Molyneaux E, Dennis CL, Rochat T, Stein A, Milgrom J. Non-psychotic mental disorders in the perinatal period. Lancet. 2014;384(9956):1775–88.
2. Stein A, Pearson RM, Goodman SH, Rapa E, Rahman A, McCallum M, Howard LM, Pariante CM. Effects of perinatal mental disorders on the fetus and child. Lancet. 2014;384(9956):1800–19.
3. Sanger C, Iles JE, Andrew CS, Ramchandani PG. Associations between postnatal maternal depression and psychological outcomes in adolescent offspring: a systematic review. Arch Womens Ment Health. 2015;18(2):147–62.
4. Murray L, Arteche A, Fearon P, Halligan S, Croudace T, Cooper P. The effects of maternal postnatal depression and child sex on academic performance at age 16 years: a developmental approach. J Child Psychol Psychiatry. 2010;51(10):1150–9.

5. Murray L, Arteche A, Fearon P, Halligan S, Goodyer I, Cooper P. Maternal postnatal depression and the development of depression in offspring up to 16 years of age. J Am Acad Child Adolesc Psychiatry. 2011;50(5):460–70.

6. Aoyagi SS, Takei N, Nishimura T, Nomura Y, Tsuchiya KJ. Association of late-onset postpartum depression of mothers with expressive language development during infancy and early childhood: the HBC study. PeerJ. 2019;7:e6566.

7. Netsi E, Pearson RM, Murray L, Cooper P, Craske MG, Stein A. Association of Persistent and Severe Postnatal Depression With Child Outcomes. JAMA Psychiatry. 2018;75(3):247–53.

8. Aoyagi SS, Tsuchiya KJ. Does maternal postpartum depression affect children's developmental outcomes? J Obstet Gynaecol Res. 2019;45(9):1809–20.

9. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, 5th edn. Washington, DC; 2013.

10. Stewart DE, Vigod S. Postpartum Depression. N Engl J Med. 2016;375(22):2177–86.

11. Guintivano J, Arad M, Gould TD, Payne JL, Kaminsky ZA. Antenatal prediction of postpartum depression with blood DNA methylation biomarkers. Mol Psychiatry. 2014;19(5):560–7.

12. Couto TC, Brancaglion MY, Alvim-Soares A, Moreira L, Garcia FD, Nicolato R, Aguiar RA, Leite HV, Correa H. Postpartum depression: A systematic review of the genetics involved. World J Psychiatry. 2015;5(1):103–11.

13. Viktorin A, Meltzer-Brody S, Kuja-Halkola R, Sullivan PF, Landen M, Lichtenstein P, Magnusson PK. Heritability of Perinatal Depression and Genetic Overlap With Nonperinatal Depression. Am J Psychiatry. 2016;173(2):158–65.

14. Stewart DE, Vigod SN. Postpartum Depression: Pathophysiology, Treatment, and Emerging Therapeutics. Annu Rev Med. 2019;70:183–96.

15. Sharma V, Doobay M, Baczynski C. Bipolar postpartum depression: An update and recommendations. J Affect Disord. 2017;219:105–11.

16. Munk-Olsen T, Laursen TM, Meltzer-Brody S, Mortensen PB, Jones I. Psychiatric disorders with postpartum onset: possible early manifestations of bipolar affective disorders. Arch Gen Psychiatry. 2012;69(4):428–34.

17. Takagai S, Tsuchiya KJ, Itoh H, Kanayama N, Mori N, Takei N, Team HBCS. Cohort Profile: Hamamatsu Birth Cohort for Mothers and Children (HBC Study). Int J Epidemiol. 2016;45(2):333–42.

18. Nakamura Y, Nakatochi M, Kunimoto S, Okada T, Aleksic B, Toyama M, Shiino T, Morikawa M, Yamauchi A, Yoshimi A, et al. Methylation analysis for postpartum depression: a case control study. BMC Psychiatry. 2019;19(1):190.
19. Kawai Y, Mimori T, Kojima K, Nariai N, Danjoh I, Saito R, Yasuda J, Yamamoto M, Nagasaki M. Japonica array: improved genotype imputation by designing a population-specific SNP array with 1070 Japanese individuals. J Hum Genet. 2015;60(10):581–7.

20. Browning BL, Zhou Y, Browning SR. A One-Penny Imputed Genome from Next-Generation Reference Panels. Am J Hum Genet. 2018;103(3):338–48.

21. Choi SW, O’Reilly PF. PRSice-2: Polygenic Risk Score software for biobank-scale data. Gigascience. 2019, 8(7).

22. Chang CC, Chow CC, Tellier LC, Vattikuti S, Purcell SM, Lee JJ. Second-generation PLINK: rising to the challenge of larger and richer datasets. Gigascience. 2015;4:7.

23. Leppert B, Havdahl A, Riglin L, Jones HJ, Zheng J, Davey Smith G, Tilling K, Thapar A, Reichborn-Kjennerud T, Stergiakouli E. Association of Maternal Neurodevelopmental Risk Alleles With Early-Life Exposures. JAMA Psychiatry. 2019.

24. Shorey S, Chee CYI, Ng ED, Chan YH, Tam WWS, Chong YS. Prevalence and incidence of postpartum depression among healthy mothers: A systematic review and meta-analysis. J Psychiatr Res. 2018;104:235–48.

25. Ahmed A, Bowen A, Feng CX, Muhajarine N. Trajectories of maternal depressive and anxiety symptoms from pregnancy to five years postpartum and their prenatal predictors. BMC Pregnancy Childbirth. 2019;19(1):26.

26. Lapato DM, Roberson-Nay R, Kirkpatrick RM, Webb BT, York TP, Kinser PA. DNA methylation associated with postpartum depressive symptoms overlaps findings from a genome-wide association meta-analysis of depression. Clinical epigenetics. 2019;11(1):169.

27. Schiller CE, Meltzer-Brody S, Rubinow DR. The role of reproductive hormones in postpartum depression. CNS Spectr. 2015;20(1):48–59.

28. Farrell C, O’Keane V. Epigenetics and the glucocorticoid receptor: A review of the implications in depression. Psychiatry research. 2016;242:349–56.

Figures
Figure 1

Depression-PRS and Bipolar-PRS in subjects with or without PPD Box plot of mean standardized Depression-PRS (a) and Bipolar-PRS (b) in subjects without PPD and subjects with “PPD at any time point.” Abbreviations: PPD = postpartum depression; PRS = polygenic risk score; N.S = not significant. **P-value < 0.01

Figure 2

Depression-PRS and Bipolar-PRS in subjects with different trajectory of PPD Box plot of mean standardized Depression-PRS (a) and Bipolar-PRS (b) in subjects without PPD, with “transient PPD,” and “persistent PPD”. Abbreviations: PPD, postpartum depression; PRS, polygenic risk score; N.S, not significant. *P-value < 0.05, **P-Value < 0.01