The association between self-reported negative stress in early life and a postpartum onset/episode of Bipolar I Disorder

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Abstract

Background. Early life negative stress can result in altered stress responsiveness later in life. This vulnerability in combination with a genetic susceptibility for psychiatric diseases can result in symptoms of a psychiatric disorder like bipolar illness. Especially when the adult has been repeatedly exposed to stress. This current study relates to the role of this stress vulnerability on the period around pregnancy. The purpose of the study was to investigate the association between self-reported negative stress in early life and a postpartum onset/episode of Bipolar I Disorder (BDI).

Methods. The research question was studied in a sample of 303 female BDI patients with children. Patients were subjected to the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) to verify the diagnosis, the Dutch edited version (JVT) of the Childhood Trauma Questionnaire (CTQ) to assess childhood trauma and the Questionnaire Postpartum Mood Disorders to assess a postpartum episode.

Results. Logistic regression showed that self-reported negative stress in early life was significantly associated with the onset of BDI (before first pregnancy or postpartum). Women who reported more negative stress in early life reported a BDI onset before their first pregnancy more often than women who reported less negative stress in early life. The occurrence of a postpartum episode was not significantly related to self-reported negative stress in early life.

Conclusions. Self-reported negative stress in early life is associated with a BDI onset before the first pregnancy. These results should be interpreted cautiously since the study has several limitations. Based on the results of the current study, self-reported negative stress in early life does not seem to be associated with the occurrence of a postpartum episode. However, the use or discontinuation of medication could not be taken into account. Since several researchers highlight the impact of discontinuation of medication on the recurrence of a postpartum episode, this association should not be immediately rejected.

Keywords. Bipolar I Disorder, Self-reported negative stress, Early life, Bipolar I Disorder onset, Postpartum onset, Postpartum episode

Introduction

For many women and their partners, the birth of a child is a joyous and exciting time. However, for some women this period is the beginning of mood swings that result in mental illness. A significant body of evidence suggests that during pregnancy and the postpartum period women have an increased vulnerability to psychiatric disorders (Fisher et al., 2012; O'Hara & Wisner, 2013; Munk-Olsen, Laursen, Pederson, Mors & Mortensen, 2007). As childbirth is a complex life event associated with numerous biological, familial and social changes, it may trigger psychiatric mood disturbances in women with predisposing genetic or psychosocial vulnerabilities (Gold, 2002).

The prevalence of Bipolar Disorder (BD) is about 1 to 2 percent in European countries (Pini et al., 2005). Out of all women with BD, 2.9% is diagnosed with postpartum BD (Vesga-Lopez et al., 2008). According to the DSM-IV, someone meets the criteria for Bipolar I Disorder (BDI) if at least one manic episode has occurred that lasts for at least one week. The manic episode is characterized by an ongoing elevated, expansive or irritable mood and impairment in at least one area of functioning. Only the occurrence of one or more manic episode is a requirement to be diagnosed with BDI, although one or more depressive episodes may occur as well (American Psychiatric Association, 2000). The disorder manifests in the adolescence and young-adulthood most frequently but it is not uncommon that the onset is at a somewhat older age (Bauer & Pfennig, 2005). Though the onset can be triggered by genetic predisposition and environmental factors and can occur at different times in a person's life, this study will focus on episodes that occur during or after pregnancy.

Despite several hypotheses, there is currently no generally accepted theory about the causes and mechanisms of postpartum mental disorders. However, the dramatic physiological events occurring after delivery have led researchers to speculate that postpartum mood disorders result from a biochemical or hormonal etiology (Hendrick, Altshuler & Suri, 1998). It is likely that this process is associated with sudden changes in the production of hormones that affect the nervous system and these changes in hormones are involved in the development of mental changes in the postpartum period. For example, removal of the placenta is associated with the removal of nearly all of the pregnancy corticotrophin-releasing hormone (CRH) (Parizek et al., 2014), a hormone that is involved in the mediation of the response to stress (Hobel, Dunkel-Schetter, Roesch, Castro & Arora, 1999). However, although it may be linked to hormonal changes, there is yet no consensus on the direct hormonal etiology. For example, research focused on postpartum depression report an absence of abnormal hormone

levels in women with postpartum depression (Bloch et al., 2000).

While etiological research on bipolar disorder is frequently focused on biological variables, the role of psychosocial factors such as stress is often overlooked (Dienes et al., 2006). Several researchers recognize that the period around pregnancy is one with an altered state of stress. Concerns of pregnant women involve the amount of social support, family support and friend support, fatigue, emotional tension, feelings of isolation, being tied down and pregnancy anxiety (Hung, 2007; Gruis, 1977; Huizink, Medina, Mulder, Visser & Buitelaar, 2002). Additional, women worry about their negative body changes and are concerned about their maternal role attainment. Thus, from a psychosocial approach, pregnancy may be considered as a specific state of high emotional tension, which can represent a potent stressor (Bjelica, 2004).

To examine the possible role of stress reactions during pregnancy, it is interesting to be aware of which part of the brain is involved with processing stress. The structure of the brain that plays a major role in controlling stress reactions, is the hypothalamic–pituitary–adrenal axis (HPA-axis). The HPA-axis is partly responsible and critical in promoting adaptive responses to stress, anxiety and fear (Sapolsky et al., 1990). During infanthood, the growing brain is highly impressionable by changes in the environment. An increased activity of the HPA-axis during adulthood might reflect a susceptibility that is programmed through early life stressful events (Rosmond, 2003). A frequently evoked HPA-axis results in excessive an enduring cortisol secretion (McEwen, 2002) and exposure to increased secretion of cortisol can result in disruption of HPA-axis regulation (McEwen, 1998). With repeated exposure to life stress, this disruption may become a vulnerability that can result in symptoms of depression and anxiety disorders (Heim, 2001). Perhaps not surprisingly, the HPA- axis has been found abnormal in psychiatric disorders, particular in major depression (Pariante & Lightman, 2008). It is plausible that adults who have had experienced negative childhood events are at increased risk for the development and persistence of different kinds of psychiatric disorders, like depression, anxiety disorders and bipolar illness as well (Heim, 2001; Post, Leverich, Xing & Weiss. 2001).

Furthermore, there is more evidence for the association between stress and a dysregulated HPA-axis. Children who grow up in families with low socioeconomic status (SES) are exposed to settings with higher population density, crime, pollution, discrimination, poor access to resources, and with hazards or privations (Baum, Garofalo & Yali, 1999). Furthermore, low-SES families experience more threatening, destabilizing and uncontrollable

life events (Bradley and Corwyn, 2002). As a result of these conditions, Lupien, King, Meaney and McEwen (2002) reported that there are significant differences in stress hormones as a function of SES (low, medium, high-SES). For example, at different ages during childhood, children with high SES present significantly lower cortisol levels than did children with low SES (medium effect size of r = -.31). It seems that SES is correlated with exposure to a stressful environment and conditions that contribute to chronic stress and that children who grow up in a low-SES family are susceptible to a chronically elevated cortisol level (Lupien et al., 2002). As earlier mentioned, there is an association between enduring cortisol secretion and a disruption of HPA axis regulation (McEwen, 1998), and this dysregulation has been found abnormal in psychiatric patients compared to healthy controls (Pariante & Lightman, 2008). For example, postpartum depression has been correlated with the chronic stressor of low SES (low effect size of r = .22) (Beck, 2001).

Taken together, preclinical and clinical studies suggest that early life stress induces long-lived hyperactivity and sensitization of several neurotransmitter systems, resulting in altered stress responsiveness (Heim & Nemeroff, 2001). These vulnerabilities may result in symptoms of depression, anxiety and bipolar illness when the adult is repeatedly exposed to life stress (Heim & Nemeroff, 2001; Post, Leverich, Xing & Weiss, 2001). Given these vulnerabilities, one would expect that women who have experienced negative stress in early life have a BDI manifestation earlier in life than their first pregnancy. This is in line with findings that individuals who experienced stress in early life report a younger age of onset of bipolar disorder than those who did not, with a difference in mean age of onset between 6 to 10 years. (Leverich et al., 2002; Dienes et al., 2006). The first hypothesis to be tested in the present study is whether there is an association between self-reported negative stress in early life and the onset of BDI; an onset before the first pregnancy or postpartum.

Though there seem to be associations between negative stress in early life and bipolar illness, the question arises whether these vulnerabilities play a role in the occurrence of postpartum BPI episode. Despite the fact that there is no consensus about the causes of a postpartum onset of mental disorder, there is consensus about the fact that women who are already diagnosed with a mental disorder before their pregnancy, have a high risk of experiencing an episode during or after their pregnancy (Harlow et al., 2007). For example, a research of Akdeniz et al. (2003) found that twenty-five to sixty-five percent of childbearing bipolar women reported a mood episode occurring at the postpartum period. This might not come as a surprise, since research has shown that stressful life events increase the risk of

recurrence of mood episodes (Moon et al., 2014). Since research shows that people who experience early life stress relapse following lower levels of stress than those with less or no early life stress (Dienes et al., 2006), it would be interesting to examine whether or not these findings are associated with mood episodes occurring at the postpartum period. The second hypothesis to be tested in the present study is whether there is an association between self-reported negative stress in early life and the occurrence of a postpartum episode in women with BDI.

In sum, there is reason to believe that there is an association between self-reported negative stress in early life the occurrence of a postpartum episode. Stressful life events can trigger the onset of BDI and the period around pregnancy is a stressful one. This way, it is plausible that women at risk can experience their first or subsequent episode of BDI around the pregnancy period. First it is expected that women with an onset before their first pregnancy have reported more negative stress in early life compared to BDI women with a postpartum onset. Second, it is expected that mothers with BDI who have had a postpartum episode have reported more negative stress in early life than mothers with BDI who have not had a postpartum episode, regardless of their onset (earlier then first pregnancy or postpartum).

Methods

Study design

The main study. The study Bipolar Genetics is a large ongoing case control study which aims to identify genes associated with Bipolar I Disorder. Bipolar Genetics is conducted by the University Medical Center in Utrecht (UMCU) in association with the University of California in Los Angeles (UCLA), which was approved by the Medical Ethics Committee (MEC) of the UMCU. The aim of the study is that after a period of 5 years, 2500 patients, 2500 relatives and 400 healthy members participated in the study.

The current sub-study. Since the current study is focused on postpartum, the data-analysis will only consist out of female patients with children who are diagnosed with Bipolar I disorder. Therefore, describing the diagnostic procedures for relatives and healthy controls will be irrelevant and not be taken into account.

Procedures

Recruitment. Several ways were used to recruit participants. Since a lot of patients with BPI

use lithium, pharmacies were instructed to send information- and invitation letters to all the lithium users in their database. Mental Health Institutions and different psychiatric treatments centers were informed about the study and asked to inform their BPI patients. The Vereniging voor Manisch-Depressieven en Betrokkenen (VMDB) also informed their members several times about the existence of the study and supported them to participate. Throughout several advertisements, newspapers, websites and magazines the awareness of the study was increased, in order to obtain participants.

Inclusion and exclusion. Once the potential participants got in touch with the study, they had to meet a number of conditions in order to be able to officially participate. All subjects had to be at least 18 years old. They must have experienced at least one full blown manic episode which was not induced by drugs or a somatic illness. Furthermore, in order to keep the group as homogeneous as possible, at least three out of the four grandparents had to be of Dutch origin. If all requirements were met, an appointment was made. Participants were excluded once the researcher found out that the IQ-score was below 80 and/or when the researcher found out that the participant was not diagnosed with Bipolar I disorder. To participate within the current study, women were required to have at least one child.

Diagnostic assessment. Before visiting the UMCU, participants received a digital interview which consisted of several questionnaires, including the Dutch edited version Jeugd Trauma Vragenlijst (JTV) of the Childhood Trauma Questionnaire (CTQ) (Bernstein, Fink, Handelsman & Foote, 1994). The JTV is a validated questionnaire that measures various forms of child abuse, including emotional neglect and abuse. Another questionnaire from the digital interview consisted was used to measure socioeconomic status. The next part of the participation was a visit to the UMCU. Some participants visited an extern location or, in special circumstances, were visited at their homes, by a researcher. The first part of the participation consisted of receiving and signing an informed consent, arranging the travel allowance and a blood sample was taken for genetic analysis. After that, a psychiatric interview was initiated.

To validate the diagnosis of the Bipolar I Disorder, a semi-structured interview for DSM-IV Axis I Disorders was administered (SCID-I, First, Spitzer, Gibbon & Williams, 1996). In the current study a Dutch version of the SCID-I was used (Van Groenestijn, Akkerhuis, Kupka, Schneider, & Nolen, 1999). All researchers have had SCID-training to adequately administer the questionnaire. During the SCID-I, participants disclosed when they experienced their first mood episode and whether this was a depressive or manic episode. The SCID-I was rated

with an acceptable interrater agreement of 0.79 (Skre, Onstad, Tongersen, & Kringlen, 1991) for Bipolar Disorder and a test-retest reliability of 0.84 (Williams, Gibbon, First, Spitzer, David, Borus, Howes, Kane, Pope, Rounsaville & Wittchen, 1992) for Bipolar Disorder.

After the SCID-I, the female patients were subjected to the Questionnaire Postpartum Mood Disorders (Bergink & Nolen, 2004). This questionnaire was used to verify if female patients experienced postpartum episodes. Furthermore, the questionnaire administered if the episode occurred during pregnancy or within which period after delivery (within 0-4 weeks, within 4-8 weeks, within 2-6 months).

Participants. In total, 655 female patients participated within the main study. Out of these women, 300 female patients were excluded from the current study since they did not met the requirement to have at least one child. Some female patients did not fully completed the JTV questionnaire (N=33) and were excluded for this reason. Female patients who did not specified the birth of their children were also excluded from the data-analysis (N=19). The final data-analysis was the result of 303 participants. See table 1 for some demographic data on these participants.

Table 1. Age and socioeconomic-status of all participants.

	BDI onset before first pregnancy (N=146)	BDI Postpartum onset (N=36)	BDI onset after first pregnancy (N=121)
Age (years), mean (SD)	48.95 (8.96)	46.58 (10.53)	54.82 (10.16)
Socioeconomic-status			
Low, *n* (%)	83 (56.8)	23 (63.9)	94 (77.7)
Medium, *n* (%)	41 (28.1)	10 (27.8)	22 (18.2)
High, *n* (%)	22 (15.1)	3 (8.3)	5 (4.1)

Statistical Analysis

The Statistical Package for the Social Sciences (SPSS, version 20.0) was used to perform the data-analysis. To test the first hypothesis (women with a postpartum BPI onset have reported less negative stress in early life compared to BPI women with an onset before their first pregnancy) a logistic regression analysis was performed. Age at first pregnancy and childhood socioeconomic status (SES) were included as covariates. Age at first pregnancy was included as a covariate since the possibility exist that an earlier age at first pregnancy gives less risk on

a BDI onset earlier then the first pregnancy. SES was included as a covariate because research suggests that low SES is associated with greater chronic stress (Baum, Garofalo & Yali, 1999). Therefore, lower SES scores can increase the possibility of a BDI onset before first pregnancy.

To test the second hypothesis (women with BPI with children who have had a postpartum episode have reported more negative stress in early life than women with BPI with children who have not had a postpartum episode) a logistic regression analysis was performed as well. Again, childhood SES was included as covariate for the same reason as with the first hypothesis. The number of children the woman gave birth to was included as a covariate since more pregnancies give more possibilities to experience a postpartum episode. The third covariate was age.

Results

Hypothesis I

The first hypothesis to be tested in the present study is whether there is an association between self-reported negative stress in early life and the onset of BDI; an onset before the first pregnancy or postpartum. A Mann-Whitney *U* test revealed no statistically significant difference in the SES-scores between women with a BDI onset before their first pregnancy (*Md* = 3, *n* = 146) and women with a postpartum BDI onset (*Md* = 3, *n* = 36), *U* = 2403.500, *z* = -.803, *p* = .422, *r* = .06. Furthermore, another Mann-Whitney U test was performed to measure the difference in age at first pregnancy between women with a BDI onset before their first pregnancy (*Md* = 31, *n* = 146) and women with a BDI postpartum onset (*Md* = 28, *n* = 36), *U* = 1780.00, *z* = -3.003, *p* = .0.003, *r* = 0.22. The results show a statistically significant difference.

Logistic regression. All assumptions were met. Hosmer and Lemeshow's chi square was not significant (*p* = .700) [χ^2 (8) = 5.531], which suggests a good fit of the model. The model as a whole explained between 8.9 % (Cox and Snell R Square) and 14.1 % (Nagelkerke R squared) of the variance in BDI onset (before first pregnancy or postpartum), and correctly classified 80.2 % of cases. JTV had a significant effect on the BDI onset. The odds ratio of negative stress in early life is less than 1, indicating that women who experienced more negative stress in early life (measured in an additional score point) are 0.95 times less likely to have a BDI postpartum onset, controlling for other factors (SES, age at first pregnancy) in the model. The covariate age at first pregnancy also had a significant effect on the BDI onset. The

odds ratio of age at first pregnancy indicates that women who are older at first pregnancy (measured in years) are 0.87 times less likely to have a BDI postpartum onset, controlling for other factors (JTV-score, SES) in the model. The results are presented in Table 2.

Table 2. Logistic Regression Analysis for variables predicting the BDI onset (before first pregnancy or postpartum), controlling for age at first pregnancy and socioeconomic-status.

					95% CI for Odds Ratio	
	B(SE)	Wald(*df*)	*p*	Odds ratio	Lower	Upper
JTV	-0.054(.23)	5.579(1)	.018*	0.948	0.906	0.991
Socioeconomic-status	-0.078(.110)	0.505(1)	.477	0.925	0.746	1.147
Age at first pregnancy	-0.137(.046)	8.870(1)	.003*	0.872	0.797	0.954
Constant	4.995(1.681)	8.834(1)	.003	147.739		

* $p < .05$

Hypothesis II

The second hypothesis to be tested in the present study is whether there is an association between self-reported negative stress in early life and the occurrence of a postpartum episode in women with BDI. The assumption of homogeneity of variances between the groups (women who have and women who have not reported a postpartum episode) was not met (p = .04). Therefore, Welch's F was used to test for age difference among groups. This difference was not statistically significant $F(1,295) = .051$, $p = .819$. A Mann-Whitney U test was performed to measure the difference in SES-scores between women who did not experienced a postpartum episode (Md = 51, n = 127) and women who did experience a postpartum episode (Md = 50.5, n = 170), U = 9515.500, z = -1.748, p = .08, r = 0.10. The assumption of homogeneity of variances of number of children between the two groups was not met (p = .02) and for that reason a Welch's F was performed to test for difference. This difference was not statistically significant $F(1,295) = .254$, $p = .609$.

Logistic regression. Again, all assumptions were met. Hosmer and Lemeshow's chi square was not significant (p = .994) [χ^2 (8) = 1.416], which suggests a good fit of the model. The model as a whole explained between 1.8 % (Cox and Snell R Square) and 2.4 % (Nagelkerke R squared) of the variance in BDI onset (before first pregnancy or postpartum), and correctly classified 58.9 % of cases. JTV had no significant effect on the occurrence of a BDI postpartum episode. The covariate age had a significant effect on the occurrence of a

BDI postpartum episode. The odds ratio of age is less than 1, indicating that woman who are older at interview date (measured in years) are 0.97 times less likely to report a postpartum BDI episode, controlling for other factors (JTV-score, SES, number of children) in the model. The results are presented in Table 3.

Table 3. Logistic Regression Analysis for variables predicting the occurrence of a postpartum BDI episode, controlling for age, number of children and socioeconomic-status.

					95% CI for Odds Ratio	
	B(SE)	Wald(*df*)	*p*	Odds ratio	Lower	Upper
JTV	-0.003(.011)	0.096(1)	.752	0.997	0.976	1.018
Socioeconomic-status	-0.098(.074)	1.737(1)	.188	0.907	0.784	1.049
Age	-0.031(.014)	5.108(1)	.024*	0.970	0.945	0.996
Number of children	-0.013(.147)	0.008(1)	.929	0.987	0.739	1.318
Constant	2.287(.989)	5.341(1)	.021	9.841		

* $p < .05$

Discussion

Main findings

The current study investigated the role of self-reported negative stress in early life on the postpartum period. It was expected that women with a postpartum BDI onset have reported less negative stress in early life compared to BDI women with an onset before their first pregnancy. Second, it was expected that mothers with BDI who have had a postpartum episode have reported more negative stress in early life than mothers with BDI who have not had a postpartum episode, regardless of their onset (earlier then first pregnancy or postpartum).

The current study support findings that indicate that individuals who reported negative stress in early life report a younger age of onset of bipolar disorder than those who did not (Leverich et al., 2002; Dienes et al., 2006). According to the current study, women who reported more negative stress in early life report a BDI onset before their first pregnancy more often than women who reported less negative stress in early life. The study also provides, with indirect evidence, that women who reported more negative stress in early life may be more prone to be exposed to stress during adulthood, as a result of altered stress responsiveness. This is in line with a growing body of evidence, that suggest that altered stress responsiveness caused by early life stress may cause vulnerabilities that result in symptoms of bipolar illness

when the adult is exposed to life stress (Heim & Nemeroff, 2001; Post, Leverich, Xing & Weiss, 2001).

The current study could not demonstrate the positive association between self-reported negative stress in early life and the occurrence of a postpartum BDI episode in women who were already diagnosed with BDI. Based on the results, it can therefore not be concluded that BDI women who reported more negative stress in early life have a higher risk to experience a postpartum BDI episode compared to women who reported less or none negative stress in early life. This is not in line with several findings that indicate that people who experience early life stress relapse following lower levels of stress than those with less or no early life stress (Dienes et al., 2006). There are several possible explanations for the absence of the expected outcome, since there are several factors that can mediate between the occurrence of stress and the way in which women are able to deal with the stress. For example, persistent pain which is accompanied by pregnancy and delivery might limit one's ability to cope with the many stressors experienced by women in the postpartum period (Eisenbach et al., 2008). Eisenbach et al. (2008) but also a systematic review of Robertson et al. (2005) reported that pregnancy- and delivery-related complications and persistent pain are associated with postnatal depression. Furthermore, a research of Webster et al. (2003) demonstrated a significant impact of a poor partner relationship on postnatal depression. Furthermore, sufficient levels of partner support acts as a protective effect for postnatal depression (Milgrom et al., 2008) as well as the support from others in the primary group. In particular positive support in the context of the event becoming pregnant, acts as a predictor of later development of depressive symptoms. This is supported by a systematic review of Robertson et al. (2005), who showed findings of numerous studies that suggest that women who do not receive good social support during pregnancy are more likely to develop postpartum depression. These findings may partly provide an explanation for the absence of the expected positive association between self-reported negative stress in early life and the occurrence of a postpartum episode.

Strengths

To our knowledge, this is one of the first studies that focused on the postpartum onset of BDI in relation to self-reported negative stress in early life, since previous studies have focused on the postpartum onset of postnatal depression or postpartum mental illness in general and not in relation to negative stress in early life. Furthermore, this current study provided research

with regard to the association between self-reported negative stress in early life and the postpartum period, which was not previously performed. Several studies investigate the association between the postpartum period and (previous) life stress, but do not take stress during infanthood into account. This way, they leave the altered stress responsiveness, as a result of negative stress in early life, out of consideration.

Limitations

The assessment of the postpartum period(s) were made retrospectively, in most cases numerous years after the period itself. However, since childbirth is a memorable moment, it is likely that this period is well remembered. Furthermore, the assessment of negative stress in early life using the JTV questionnaire was a self-report measure. The scores could be influenced by the present state of the respondent. For example, when the respondent is in a depressive state at the time of participation, a negative retrospective bias could provide for a higher score on the JTV questionnaire. Another limitation of the current study is the fact that use or discontinuation of medication could not be taken into account as a covariate. Assessment included a lithium questionnaire, but since its retrospective nature this questionnaire was not taken into account as a precautionary measure for unreliability. This is one of the main limitations of the study since several researchers highlight the impact of discontinuation of this medication on the recurrence of a postpartum episode (Viguera et al., 2000; Viguera et al., 2007). Moreover, discontinuation of maintenance pharmacologic treatment in general is associated with high rates of relapse. Unfortunately, the current study did not provide information concerning general pharmacological treatment during pregnancies.

Implications for further research

This study showed that individuals who reported more negative stress in early life are associated with an earlier age of onset of bipolar disorder than a postpartum onset, which may indicate that a BDI postpartum onset is less influenced by stress than a BDI onset before the first pregnancy. This onset might be more biologically/genetically grounded than environmental factors, which gives prospects for future research. Future research could begin with including family psychopathology in order to examine genetic predispositions. Family psychopathology of closely related family members could not only account for a genetic predisposition, but might also be responsible for an increased stress level for the mother

during pregnancy. This should be taken into consideration as well.

As earlier mentioned, this study did not take into account several other (psychosocial) factors besides the occurrence of negative stress in early life. These other factors (partner relationship and support, social support, use and/or discontinuation of medication, obstetric factors) have shown their impact on at least one type of bipolar episode, namely a depressive episode. It would be interesting to replicate this study and involve the aforementioned factors in order to constitute a more complete view of the impact of various psychosocial factors. Furthermore, since previous research have mainly focused on postnatal depression, future research should focus more on the association between bipolar disorder and the postnatal period in order to increase knowledge about possible risk factors on postnatal illness for women who are diagnosed with bipolar disorder. Further research should include the use and/or discontinuation of medication as a covariate in order to re-examine the role of negative stress in early life on the occurrence of a postpartum BDI episode. Also, although 303 people participated within this current study, only 36 women had a postpartum onset BDI. A larger trial of this group of women is warranted to replicate the promising findings from this study.

It is important to perform extended studies on this current study in order to provide insight in the emotional well-being of pregnant women who experienced negative stress in early life. This way, nursing and other interventions can be better informed during the vulnerable period around pregnancy. Furthermore, it is not only important for the women to perform extended studies but also for the offspring since maternal stress can partly determine the behaviour of the offspring (Weinstock, 2008).

Conclusion

On the basis of this current study, one could conclude that self-reported negative stress in early life is associated with a BDI onset at a young age, before the first pregnancy. However, since the limitations mentioned, this result should be interpreted cautiously. The negative correlation between self-reported negative stress in early life and a postpartum BDI onset found in this study, could possibly indicate for the role of biological influences. Furthermore, this current study disclaimed the association between self-reported negative stress in early life and the occurrence of a postpartum episode. Since the limitations mentioned, this association should not be immediately rejected. Further research is required.

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