UNICOS

DOI: https://doi.org/10.5281/zenodo.7400409

MINI REVIEW

Postpartum depression: A mini-review

Sena Inal Azizoğlu

Başakşehir Çam and Sakura City Hospital, Department of Psychiatry, Istanbul, Turkey

Abstract

Stress and traumatic past experiences are two of the main risk factors for the development of postpartum depression. Reprogramming of the HPA axis and epigenetic alterations, which can also affect HPA function, are two neuroendocrine changes reported in postpartum depression that is linked to stress and negative life events. Because it is well established that stress hormones affect neuroinflammation, altered HPA axis function may have an impact on peripartum neuroimmune alterations that affect postpartum depression. On the other hand, neuroinflammation can affect how well the HPA axis functions, which may possibly be a factor in postpartum depression. By highlighting both clinical and fundamental science research findings, this review attempts to highlight the numerous potential pathophysiological pathways that contribute to postpartum depression. The discussion of postpartum depression risk factors may reveal information regarding potential neurological causes. The biology of postpartum depression is examined along with the evidence that suggests the involvement of neuroendocrine alterations, neuroinflammation, altered neurotransmitters, circuit malfunction, genetics, and epigenetics. This review emphasized neuroendocrine changes.

Keywords: Anhedonia, depression, post-partum, stress.

Correspondence:

Inal Azizoğlu S, Başakşehir Çam and Sakura City Hospital, Department of Psychiatry, Istanbul, Turkey.

e-mail: mdsazizoglu@gmail.com

Specialty section:
This article was submitted to the Psychiatry section

Received: 10 October 2022
Revised: 30 October 2022
Accepted: 13 November 2022
Published: 5 December 2022

Introduction

A serious depressive episode that is temporally connected to childbirth is referred to as a postpartum depression. The American Psychiatric Association changed the name of this disease to peripartum depression in 2013 Diagnostic and Statistical Manual of Mental Disorders (DSM-V) and now specifies that the commencement of mood disturbance might occur during pregnancy or within four weeks of childbirth (1,2). One of the most frequent problems of the postpartum period, peripartum depression affects 15-20% of childbearing women annually and results in 600,000–800,000 occurrences of the condition (3) (Table 1).

Peripartum depression is a potentially fatal condition that has lasting effects on both moms and their offspring. There are long-term hazards connected with postpartum depression in addition to the pain and disability it causes, such as an increased chance of peripartum and non-peripartum depression recurrence

and an increased disease burden with successive depressed episodes. In addition, children of moms who experienced peripartum depression are more likely to experience behavioral issues and developmental impairments (4,5).

Table 1: DSM-5 Diagnostic criteria for major depressive disorder

For a diagnosis of major depressive disorder, 5 or more of the following symptoms must be present nearly every day for at least a 2-week period. Symptoms must impair functioning and cannot be secondary to another drug or illness.
*** Depressed mood loss of time and on most days** *** Anhedonia** *** Significant change in weight (weight loss or weight gain** *** Sleep disturbances (insomnia or hypersomnia)** *** Psychomotor fluctuations** *** Change in energy levels (fatigue, loss of energy)** *** Excessive guilt or feelings of worthlessness** *** Difficulties concentrating** *** Recurrent thoughts of death or suicidal thoughts**
Peripartum onset specifier: Onset of symptoms occurs during pregnancy or within 4 weeks after childbirth. Episodes can present psychotic features.

Information is provided on the pathophysiology of postpartum depression, including information on neuroendocrine changes, neuroinflammation, the neurotransmitter system, circuit dysfunction, and the involvement of genetics and epigenetics. We shall briefly discuss the neuroendocrine process in this review.

Hormone levels undergo sudden and severe fluctuations throughout the peripartum period. Mood disorders are also more likely to develop during this time, and it is believed that these two processes are connected in that changes in reproductive hormones may have an impact on the neurobiology of postpartum mood disorders. This idea has given rise to the "ovarian-steroid-withdrawal hypothesis" (6). The underlying neurobiology of postpartum mood disorders has also been linked to neuroendocrine anomalies, such as higher stress hormone levels during the peripartum period. Focusing on the involvement of ovarian and lactogenic hormones (estrogen, progesterone, oxytocin, and prolactin) as well as stress hormones (cortisol, ACTH, and CRH) and their neurosteroid metabolites, we will examine the data suggesting a role for neuroendocrine abnormalities in postpartum depression (Figure 2). We will also draw attention to how reproductive hormones interact with one another, as these interactions have been found to affect HPA axis function and vice versa (6).

There are no consistent changes in hormone levels, the kinetics of hormone withdrawal, or larger fluctuations associated with postpartum depression (8), which is likely due, in part, to inherent variability in the patient population as well as methodological variations between studies. However, it is challenging to discount the possible significance of these hormonal oscillations given that the timing of symptom onset coincides with large changes in the levels of reproductive hormones. Women with postpartum depression may not have different absolute hormone levels, but they may have greater sensitivity to changes in reproductive hormones at the brain's level. According to a significant study, estradiol and progesterone withdrawal only causes depression scores to rise in women who have already experienced postpartum depression, suggesting that these women's brains may react differently to hormonal changes. Animal research, where these variables may be more controlled than in a clinic, provide additional evidence for the role of reproductive hormones in postpartum depression (9).

Stress hormones (Cortisol, ACTH, CRH)

It has been suggested that postpartum depression's underlying neuropathology is caused by dysfunction of the HPA axis (9). This is due in part to the fact that neuroendocrine disruptions are one of the most often observed symptoms of major depressive disorder and stress is a significant risk factor for postpartum depression (10). There is evidence of altered levels of cortisol, ACTH, and CRH in postpartum depression patients, which is consistent with a role for HPA axis dysfunction in the condition (9). Even indicated as a diagnostic criterion for postpartum depression is elevated levels of CRH (11).

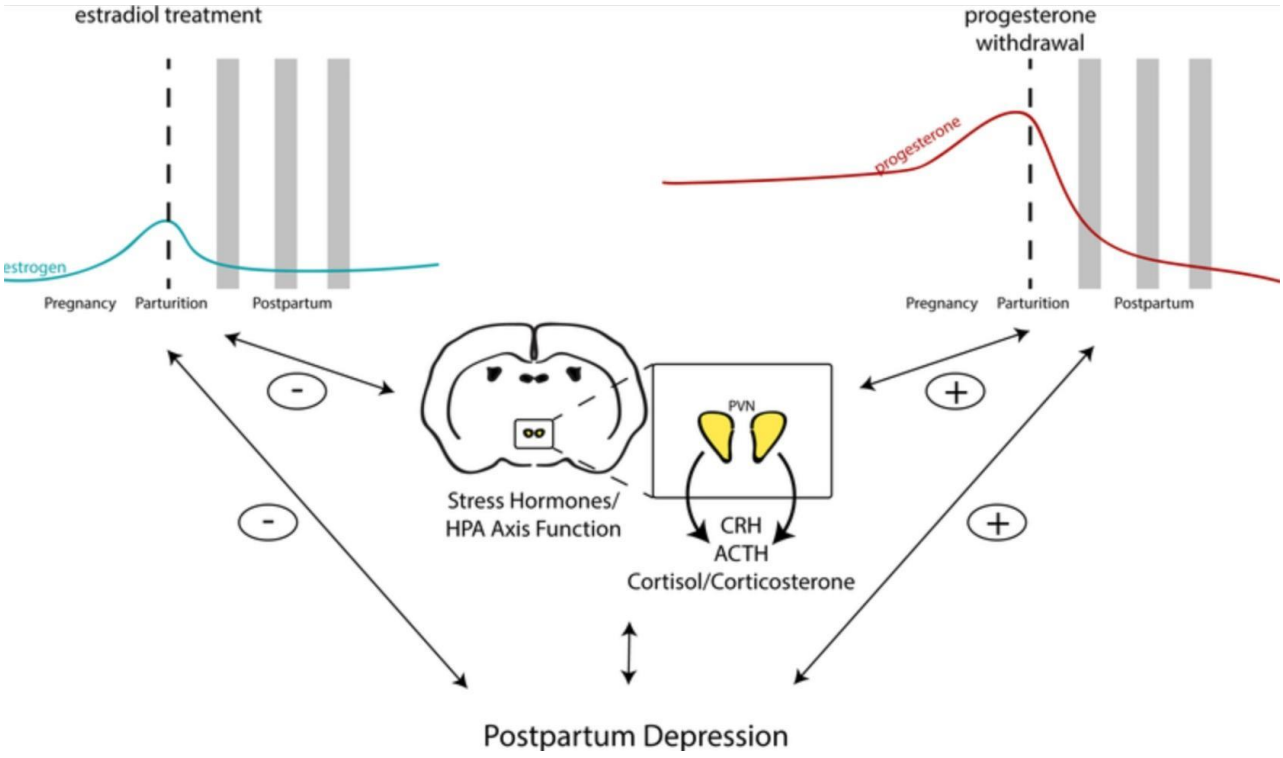

Figure 1: Crosstalk between the HPG and HPA axes in postpartum depression (7).

These claims, however, are still debatable and there is yet no proof that the HPA axis contributes to postpartum depression (12,13). Decreased reactivity to the dexamethasone suppression test and an altered ACTH-to-cortisol ratio (14) are two signs that the control of the HPA axis may be faulty in women with postpartum depression. Interesting findings suggest that withdrawal from gonadal steroid levels improves HPA axis function, especially in women with a history of postpartum depression, as seen by the increase in stimulated cortisol seen in these women (15). However, there are discrepancies in this literature, with some studies not supporting HPA axis dysfunction in postpartum mood disorders (13). To resolve these conflicting reports, additional research has been called for (12).

Unfavorable life events are believed to change how the HPA axis functions, making people more susceptible to mood disorders. As a result, the findings suggest HPA axis malfunction in postpartum depression may be an epiphenomenon linked to the elevated risk in individuals who had experienced negative life experiences in the past. Accordingly, early life stress has been shown to cause HPA axis reprogramming in experimental animal models. It has also been demonstrated to increase depressive-like behaviors in the postpartum period and to cause deficits in maternal care (16,17).

Experimental data showing that chronic stress paradigms during pregnancy or breastfeeding are sufficient to cause depressive-like behaviors in postpartum mice and impair maternal behaviors provides direct evidence in favor of a role for HPA axis malfunction in postpartum depression. Since exogenous corticosterone is given during pregnancy and/or the postpartum period and also causes depressive-like behaviors in postpartum animals and reduced maternal behaviors, the effects are probably mediated by the stress hormone corticosterone. In a mouse model of postpartum depression, inhibiting CRH signaling with antalarmin also reduces depressive-like behaviors (18-20).

Conclusions

This review demonstrates how closely related the hypothesized neurobiological mechanisms for postpartum depression are. These include a variety of

potential pathological mechanisms, including disruptions in reproductive and lactogenic hormones, stress and HPA axis dysfunction, neuroinflammation, synaptic transmission, epigenetics, and circuit-level alterations in network communication. These many pathways suggest that there may be a number of mechanisms mediating the emergence of a widespread pathophysiological signature connected to postpartum depression. Understanding the neurobiology behind normal maternal care and behavior as well as the pathophysiology of postpartum depression may help us better understand postpartum depression.

Conflict of interest:

The authors report no conflict of interest.

Funding source:

No funding was required.

Ethical approval:

No need for reviews.

Contributions

Research concept and design: **SIA**
Data analysis and interpretation: **SIA**
Collection and/or assembly of data: **SIA**
Writing the article: **SIA**
Critical revision of the article: **SIA**
Final approval of the article: **SIA**

References

1. Epperson CN. Postpartum major depression: Detection and treatment. Am Fam Physician. 1999;59(8):2247–54.
2. Logsdon MC, Usui W. Psychosocial predictors of peripartum depression in diverse groups of women. Western Jrnl of Nurs Res. 2001;23(6):563–74.
3. Hay DF, Pawlby S, Angold A, Harold GT, Sharp D. Pathways to violence in the children of mothers who were depressed postpartum. Dev Psychol. 2003;39(6):1083-94.
4. Logsdon MC, Wisner KL, Pinto-Foltz MD. The impact of peripartum depression on mothering. J Obst, Gyn, and Neo Nurs. 2006;35(5):652–8.
5. Beck CT. The effects of peripartum depression on child development: A meta-analysis. Arch Psych Nursing. 1998;12(1):12–20.
6. Bloch M, Schmidt PJ, Danaceau M, Murphy J, Nieman L, Rubinow DR. Effects of Gonadal Steroids in Women With a History of Postpartum Depression. Am J Psychiatry. 2000;157(6):924-30.
7. Payne JL, Maguire J. Pathophysiological mechanisms implicated in postpartum depression. Front Neuroendocrinol. 2019;52:165-180.
8. Schiller CE, Meltzer-Brody S, Rubinow DR. The Role of Reproductive Hormones in Postpartum Depression. CNS Spectr. 2015;20(1):48-59.
9. Bloch M, Daly RC, Rubinow DR. Endocrine factors in the etiology of postpartum depression. Compr Psychiatry. 2003;44(3):234-46.
10. Pariante CM, and Lightman SL. The HPA axis in major depression: classical theories and new developments. Trends Neurosci. 2008;31(9):464-8.
11. Yim IS, Glynn LM, Dunkel-Schetter C, Hobel CJ, Chicz-DeMet A, Sandman CA. Risk of postpartum depressive symptoms with elevated corticotropin-releasing hormone in human pregnancy. Arch Gen Psychiatry. 2009;66(2):162-9.
12. Rich-Edwards J, Hacker M, Gillman M. Premature recommendation of corticotropin-releasing hormone as screen for postpartum depression. Arch Gen Psychiatry. 2009;66(8):917.
13. Meltzer-Brody S, Stuebe A, Dole N, Savitz D, Rubinow D, Thorp J. Elevated corticotropin releasing hormone (CRH) during pregnancy and risk of postpartum depression (PPD). J Clin Endocrinol Metab. 2011;96(1):E40-7.
14. Jolley SN, Elmore S, Barnard KE, Carr DB. Dysregulation of the hypothalamic-pituitary-adrenal axis in postpartum depression. Biol Res Nurs. 2007;8(3):210-22.
15. Bloch M, Rubinow DR, Schmidt PJ, Lotsikas A, Chrousos GP, Cizza G. Cortisol response to ovine corticotropin-releasing 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(2):695-9.
16. Murgatroyd CA, Nephew BC. Effects of early life social stress on maternal behavior and neuroendocrinology. Psychoneuroendocrinology. 2013;38(2):219-28.
17. Murgatroyd CA, Peña CJ, Podda G, Nestler EJ, Nephew BC. Early life social stress induced changes in depression and anxiety associated neural pathways which are correlated with impaired maternal care. Neuropeptides. 2015;52:103-11.
18. Carini LM, Murgatroyd CA, Nephew BC. Using chronic social stress to model postpartum depression in lactating rodents. J Vis Exp. 2013;(76):e50324.
19. Maguire J, Mody I. Behavioral Deficits in Juveniles Mediated by Maternal Stress Hormones in Mice. Neural Plast. 2016;2016:2762518.
20. Kara A. A review of childhood anxiety. J Clin Tri Exp Invest. 2022;1(3):64-70.