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Editorial

Postpartum Depression – From Evolutionary Concepts to Neuropsychoendocrinological Backgrounds and New Treatment Medications

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Both the bipedal locomotion about 4.4 million years ago, including the decreased pelvic circumference and narrowed vaginal tract, and the rapid brain expansion about 500,000 years ago, led to the so-called obstetric dilemma [1]. With this, both pregnancy and childbirth have become strenuous and risky [2]. As a result, and to cope with such strain, a few days after delivery, 40%–80% of mothers suffer from symptoms of depression ("baby blues") [3], and about 17% [4] to 20% of mothers are suffering from postpartum depression (PPD) in the first six months following delivery [3,5,6,7,8,9]. Importantly, within the context of evolutionary psychology and psychiatry, a depressive phase is considered an adaptive process to preserve energy, to withdraw from challenging social interactions, and to enhance the efforts and resources of the social environment [10,11,12]. Typically, females with PPD report a wide variety of symptoms such as sad and depressed mood, emotional tension, agitation, irritability, social and interactional withdrawal, feelings of worthlessness and guilt, severe sleep disturbances, and signs of suicidal behavior [3,13]. Likewise, mothers with PPD might show less responsivity and sensitivity to the newborn's behavior and interactional efforts [3]. Given this, PPD fulfills the criteria of a major depressive disorder, with the onset within four weeks after delivery [13].

To explain the emergence and maintenance of PPD, in the present Editorial, we focus on (1) evolutionary psychology and psychiatry, and (2) neuroendocrinological research, including (3) two novel medication options.

1. Evolutionary Psychology and Psychiatry and Postpartum Depression (PPD)

Concepts of evolutionary psychiatry have gained increased scientific attention [14]. From the viewpoint of evolutionary psychology [9,12,15,16,17,18] and evolutionary psychiatry [10], in ancestral times, PPD is considered the young mother's strategy to promote the reallocation of limited resources after a physically and psychologically demanding pregnancy and childbirth to self-preservation [10]. More specifically, and considering the evolutionary context of small-scale societies of about 120–150 individuals with kin-based organizations [19], the mother's withdrawal from the social and economic activities implies high costs on the other group members. By contrast, the manifestation of symptoms of clinical depression is also an honest and credible signal to the kin members that cooperation is currently not possible. Furthermore, other females (the allomaternal support shared caregiving of sisters, grandmothers, aunts, or female cousins) of such kin-based societies could care for the newborn, including breastfeeding. Given this context, from the viewpoint of evolutionary psychology and psychiatry, PPD is considered an explicitly favorable adaptation to the constraints of survival. However, the contrast between evolutionary adaptive processes and our current lifestyle mirrors what is called evolutionary mismatch [20]. Given this, the lack of social and partner support [12,15,16,21,22] as a psychosocial risk factor for PPD further substantiates the evolutionary mechanisms of PPD. To support this assumption, the prevalence of postpartum depression or distress is much lower in today's typical hunter-gatherer societies, such as the Hadza in Tanzania [23]. Regarding the development of the newborn, it is plausible to assume that in ancient times, above

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all, the allomaternal support and shared caregiving provided the newborn with breastfeeding, warmth, and calming, responsive behavior. By contrast, and taking into consideration the evolutionary mismatch and current lifestyle behavior mostly characterized by a two-parent family system, there is evidence that the mother's postpartum depression is associated with an unfavorable mother-child interaction (see [24] for a systematic review and meta-analysis). Dou et al. [25] observed among 686 mother-child pairs that higher scores for mothers' postpartum depression were associated with lower scores for infants' communication styles, gross- and fine-motor skills, prosocial behavior, and overall cognitive, emotional, behavioral, and interactional development at the age of 12 months. Overall, there is sufficient evidence that today's mothers' postpartum depression is associated with more cognitive, emotional, behavioral, and social/interactional developmental issues of the offspring.

2. Results From Neuroendocrinological Research

Physiologically, there is a gradual rise of steroid hormones during pregnancy and a steep decline in postpartum. However, trajectories of hormonal adaptations seem to differ in females who develop PPD: Prenatal lower cortisol concentrations predicted the odds of suffering from PPD, though studies vary regarding assessment methods, time points, and lab analysis [26]. The dynamics of the hypocortisolism-PPD link are very similar to what has been observed among individuals suffering from post-traumatic stress disorder (PTSD) [27], where the organism drops to a state of generalized psychophysiological dysfunctionality. To illustrate this concept, Sadeghi-Bahmani et al. [28] assessed 129 mothers three days and 12 weeks after delivery. Participants provided hair strands for the analysis of hair glucocorticoid concentrations 12 weeks before and 12 weeks after delivery. Pre- and postpartum lower hair cortisol in relation to hair cortisol correlated with exposure to prenatal stress and higher PPD symptom scores. Jahangard et al. [29] assessed 48 females with PPD and 50 healthy controls. All participants provided hair strands to assess hair steroids (e.g., cortisol, cortisone, progesterone) 12 weeks before and 12 weeks after delivery. Compared to females without PPD, females with PPD had statistically significantly lower cortisol, cortisone, and progesterone concentrations both during the last trimester and 12 weeks after delivery. In addition, lower prenatal hair cortisone and lower prenatal hair progesterone levels predicted higher depression scores 12 weeks after delivery. Finally, there is accumulating evidence that low concentrations of progesterone and allopregnanolone (the latter is a metabolite of progesterone) are associated with higher scores for anxiety and depression during postpartum [30].

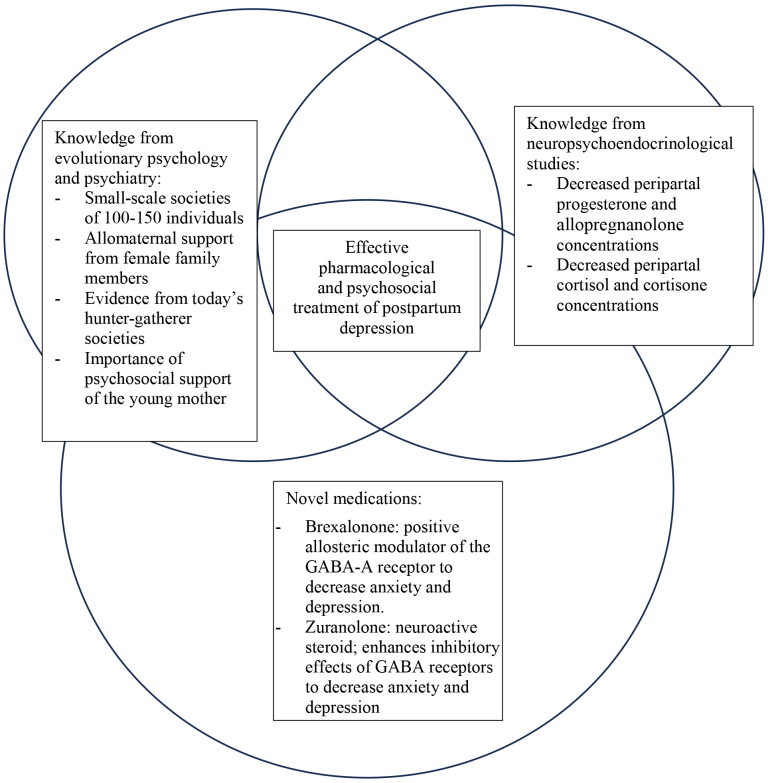

Fig. 1. Three dimensions to explain the emergence and dynamics of postpartum depression from the view point of evolutionary psychiatry and psychology, from neuroendocrinological research, and from novel medication treatments.

3. Two Novel Medications

The observation of significantly lower progesterone concentrations [30], along with allopregnanolone, in females with PPD has led to the formulation of two novel medications:

First, Brexanolone is chemically identical to allopregnanolone. It is a positive allosteric modulator of the GABA-A receptor and decreases symptoms of anxiety and depression. Brexanolone is administered intravenously for 60 consecutive hours, and symptoms of PPD decreased after 2.5 days and remained consistently low over 30 days [31,32,33].

Second, Zuranolone is an orally administered neuroactive steroid, which is a synthetic compound directly derived from allopregnanolone, and which also enhances the inhibitory effects of GABA receptors, leading to decreased symptoms of anxiety and depression. Beneficial effects are observed as early as the third day after administration, and the decreased levels of depression remain stable over 40 days [34,35,36].

In our opinion, both concepts of evolutionary psychology and psychiatry and neuroendocrinology complement each other and offer a comprehensive explanation of the emergence, maintenance, and treatment of postpartum depression. Novel pharmacological treatment opportunities offer the possibility to treat PPD more effectively (see Fig. 1). On a practical and behavioral level, concepts of evolutionary psychiatry and psychology suggest that the young mother should establish a broad, solid, and trusting social network of relatives and peers from the very beginning of pregnancy. The consequences of low levels of progesterone, allopregnanolone, and cortisone imply that women are more vulnerable to stress with symptoms of anxiety, while their hypothalamic–pituitary–adrenal (HPA) axis is still inflexible to functionally cope with stress challenges. This is in line with the above-mentioned hypothesis that vulnerable postpartum females depend on a protective and nursing social environment. Complementarily, the two novel allopregnanolone-like medications Brexanolone and Zuranolone might ameliorate the (patho) physiologic gap between the challenge of pregnancy and labor, and the cognitive-emotional and behavioral capability during the early postpartum period.

Author Contributions

DSB, TM and SB contributed to the conceptualization and the writing of the present paper. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

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Conflict of Interest

The authors declare no conflict of interest.

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