

The Biological Mechanism of Maternal Depression's Negative Influences on Offspring Development: A Review

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Abstract—Maternal depression is a prevalent disorder among mothers: nearly 20% of women have experienced different levels of depressive symptoms during motherhood. The symptoms usually disappear by three years after their children were born, but some women experience them chronically. Maternal depression has been researched in terms of its negative influence on offspring since the 1960s. Children of chronically depressed mothers show delays in cognitive, emotional, and behavioral development. Moreover, they may even face mental health challenges themselves. How does maternal depression influence offspring? Previous studies have focused on the behaviors of mothers and found that mothers with depression interact with their children in a less engaging way. Recently, more researchers started to pay attention to the biological mechanism of this maternal depression's negative influence. Cortisol, a hormone associated with stress, is regarded as a potential pathway of the transgenerational transmission of depression. Mothers with prenatal depression have elevated cortisol level during pregnancy, which is passed down to their children. After they are born, children of depressed mothers react to stress with more dramatic changes in cortisol level and compromised stress-coping abilities. Moreover, prenatal maternal depression also seems to shape the functional connectivity of amygdala, a brain area related to stress and emotions. For life situations like schooling, competing with peers or making significant decisions, children with decreased or abnormal stress-coping abilities will be in disadvantageous positions. Attenuated stress coping abilities brought by hormonal and neural changes may be a biological mechanism for children's lower performance in cognitive and behavioral tasks.

Index Terms—cortisol, maternal depression, offspring development, stress

I. INTRODUCTION

Motherhood is not easy, and it can be a challenge both physically and emotionally. Pregnant women not only have to bear with weight changes and increasing daily inconveniences like restricted diet and lack of sleep, many of them also suffer from unstable emotional states and even mental disorders. In fact, 6.9% to 20% of pregnant women experience severe depressive symptoms. After child deliverance, 10% to 15% mothers experience postpartum maternal depression, and it may last throughout their lifetime [1]. In addition to the maternal depression's substantial prevalence and serious effect on mothers, another concerning factor is that maternal depression can have significant negative influence on offspring development. Studies show

that maternal depression may influence children's social and language development through different parenting behaviours and everyday mother-child interactions. For example, children of depressed mothers are less likely to get consistent responses from their mothers and to develop secure attachment type [2].

Although most previous studies have focused on how mothers' depressive symptoms in social interactions influence offspring development, these effects are not as substantial as expected in longitudinal studies: they can be adjusted through interventions designed to improve parenting style of depressed mothers and their interactions with offspring [3], [4]. However, recent studies start to pay more attention to the biological effects of maternal depression. For example, depressed pregnant women tend to release higher levels of stress-related hormones, which may delay fetus development prenatally, before any mother-infant interactions even take place [5]. In fact, infants whose mothers have depressive symptoms during pregnancy are more likely to be born immature and underweight. This process, known as the programming effect, can even directly influence offspring's biological architecture, shape their developmental trajectories, and increase future risks of psychopathy or neurological disorders [6]. For example, experiencing elevated stress-related hormones in uterus may alter offspring stress coping abilities through the hypothalamic-pituitary-adrenal (HPA) axis [7]. Stress coping abilities matter for school performance and navigation through complicated social environment in adulthood. In this way, the negative biological effects of maternal depression may also set children up for delays in offspring social and cognitive development.

Biological influences are more long-lasting and harder to intervene than merely behavioural ones, as some physiological changes may be irreversible. Prenatal anti-depression medication has been shown to lessen programming effect by suppressing the amount of stress-related hormones during pregnancy [8]. It is known that maternal depression influences offspring development negatively in various ways, but the specific mechanisms remain unclear. We suggest future studies to focus on the biological mechanisms of depressive symptoms' transgenerational transmission from mothers to their offspring, and the connections between biological changes and cognitive or behavioural delay in offspring. These investigations will help develop more efficient interventions alleviating the negative effects of maternal depression on offspring.

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II. INFLUENCE ON OFFSPRING DEVELOPMENT

Maternal depression influences offspring development negatively from prenatal to postnatal, physiologically, cognitively and emotionally. Children of mothers with depression have higher risk of cognition development deficit or delay. Experiments found that infants of depressed mothers have higher risks of depression, conduct disorders, and attention disorders [9]. They are also more likely to have difficulties in maintaining friendly social interactions, sharing, and helping others. These effects are related to the way depressed mothers interact with their children. For example, depressed mothers are more likely to fail to elicit infants' attention or to not respond to infant behavior [10]-[12]. However, maternal depression can have an impact on offspring even before they are born. Research shows that mothers with depression are more likely to come from disadvantageous living environments where there is increased substance use and higher distress during pregnancy. They are more likely to experience other stressors, such as financial hardship, being a single mother or social isolation. This stressful environment may increase the risk of infant premature birth and lower birth weight [13], [14]. Importantly, birth weight is shown to be positively associated with cognitive and language development [15]-[17]. In this way, maternal depression affects infant development through physical to mental delays. In addition to that, maternal depression influences offspring's biological development before birth through increased levels of stress-related hormones, like cortisol [7]. It is also associated with structural changes in left amygdala, a key brain region involved in the activation and regulation of emotional states [6]. Through hormonal and neural changes, offspring may also experience struggles with emotional regulation.

A. Influence Through Social Interactions and Attachment

It has been suggested that the symptoms of depression such as low mood, low energy, loss of interest, helplessness, irritability or excessive concern towards children [18]—prevent mothers from offering an optimally sensitive interaction with their children. In other words, the parenting behaviors of depressed mothers are altered and regulated by depression. Thus, they fail to respond actively and effectively, or to maintain high levels of attention to their children. They engage children with activities or play significantly less often [19]. These disadvantageous parenting styles decrease the chance for infants to develop secure attachments with their mothers. Instead, they are at a higher risk of developing Avoidant or Disorganized types of attachment. Disorganized attachment is a strong predictor of later externalizing problems and cognitive delay [2]. Moreover, the behaviors of depressed mothers are more likely to be hostile and coercive. Growing up in this kind of environment, children are more likely to have emotional and behavioral issues [20], and show significantly more depressive symptoms before puberty [7]

B. Negative Effects on Cognitive and Language Development

As mentioned above, disengagement and lower quality of interaction are prevalent between depressed mothers and their children. The lack of high-quality interaction gives rise to not only insecure attachment and adverse social abilities, but also

delay in development of language and cognition. Children of depressed mothers demonstrated a decline in age expected cognitive skills while those of non-depressed mothers showed age expected increases [3]. Although the delay in cognition development can be improved by using Toddler-Parent Psychotherapy (TPP) [3], still children with depressed mothers showed lower verbal IQ scores. On top of that, the interaction between depressed mothers and children also influences the development of language. When mothers speak to their infants, they use child-directed speech, a special intonation pattern which has inflated fundamental frequency, greater amplitude, simplification of vocabulary and more repetition [21]-[23]. This special speech style is essential to infant language development. However, depressed mothers use child-directed speech significantly less, and even when they use it, their child-directed speech fails to promote associative word learning [24]. More specifically, infant associative word learning based on mothers' child-directed speech is negatively associated with mothers' self-reported depression severity level. This shows that the quality of child-directed speech produced by mothers with more serious depressive symptoms is compromised, which fails to draw infants' attention.

Despite ample evidence on maternal depression and delayed offspring cognitive and language development, there are also contradictory observations. In Piteo and colleagues' study in 2012 [25], they found no association between poorer infant development and postnatal depression in the first 6 months after infants were born. The cognitive, language and motor development of infants of mothers with depression, at 6 weeks and then at 6 months, are not significantly different from those of mothers without depression. It may be true that not all maternal depression will cause developmental delay. However, future studies should investigate how severity of depression mediate its negative effects on offspring development, and especially pay attention to mothers with chronic and severe depressive symptoms.

C. Negative Effects Through Biological Mechanisms

The primary stress-related hormone we mentioned above that affects offspring development prenatally is called cortisol. Cortisol is a hormone that makes people feel nervous, anxious or even angry, and a quick increase and decrease of it is characterised as physiological reaction of stress. Cortisol is released by hypothalamic-pituitary-adrenal (HPA) axis, a critical adrenocortical system that controls responses to stress and also regulates the immune system, emotions, sexuality and digestion [26]. Pregnant mothers with depression have higher levels of cortisol. As a result, their infants, whose growths are shaped by the environment in the uterus, have elevated cortisol levels too, even months after they are delivered [27] [28] [29]. For example, infants of comorbid mother with depression and anxiety have higher cortisol production over the day and bedtime at 6 months of age [30]. Constantly or easily increased cortisol level may exhaust the HPA axis system, which is detrimental to infants' stress coping abilities and emotional regulations. In de Weerth and colleagues' study, higher mother prenatal cortisol levels were shown to predict more infant negative facial expressions, crying and fussing, during mother-infant interactions up to 5 months of age [26]. However, this effect in dramatic reactions

to stress does not go away with development. Children with chronically depressed mothers show lower baseline cortisol in non-stressful situations, and a more dramatic cardiovascular response to acute stress at the age of 9.5 [7]. The same study also found that child's cortisol

level is also associated with maternal depressive symptoms. Children with normal initial cortisol levels have mother with gradually declining depressive symptoms over years, whereas children with abnormally lower baseline cortisol level have mothers with chronic depression with little change over time. In another study [31], although no evidence about the connection between infant cortisol level and postpartum anxiety was found, infant stress reactivity and prenatal maternal stress was found to be significantly correlated.

In addition to infant abnormal hormonal and cardiovascular reactions to stress, evidence of maternal depression's negative influences in the neural connectivity level was also found. Amygdala, known as the core of fear processing, is an essential brain region that regulates emotional responses including fear, anxiety and aggression, and controls stress reactivity. It also has an important role in the memory processing and decision-making process. Notably, studies show that at 6 months of age, infants of mothers with severe prenatal maternal depression form amygdala connectivity patterns similar to those seen in adults with depression [6]. Infants at 6 months of age already have well developed functional connectivity among brain regions. This is especially concerning as it suggests that infants' abnormal neural connectivity may not be altered. This neural effect is indeed long-lasting: another study shows that prenatal maternal depression predicts increased amygdala volume in 7-year-old offspring [32], while enlarged amygdala predicts major depression [33]. Through this biological pathway, depressive disorder passes down from mothers to offspring and to more generations, even if mothers make tremendous amounts of efforts to change their parenting styles on a behavioral level. Finally, the influences in hormonal and neural domains are not independent from each other but intertwined. Higher cortisol level is also associated with a larger amygdala volume, when both are associated with depressive symptoms [33]-[35]. This finding underscores the complexity and irreversibility of biological influences of maternal depression.

D. Lasting Influence Over the Years

How long will the negative effects of maternal depression last? In a longitudinal study [30], 6 months old infants of comorbid mothers with depression and anxiety have higher cortisol levels compared to both infants of depressed and non-depressed mothers. However, at the age of 18 months, the difference goes away, which may be explained by the developmental plasticity of infant HPA axis. The effect of maternal depression on language development delay can be detected at a very early age, which means that behavioral intervention can take place as early as possible to prevent or attenuate the delay. Although depressed mothers are found to be less responsive or sensitive during interactions with young infants, a study found no quality difference in mother-child interactions between mothers with depression and without when children are at preschool age [31].

Nevertheless, other studies show that the negative

influences may be long-standing. For example, a study by Gump and colleagues on 9.5-year-old children shows that the effects of maternal depression on cardiovascular, adrenocortical, and emotional functioning last at least until puberty [7]. Moreover, amygdala functional networks do not change much throughout a lifetime. Thus, the influence of maternal depression on left amygdala functional connectivity can persist into later life until adulthood and increase the risk of depression [7]. Even on a purely behavioral level, maternal depression predicts conduct problems in offspring, both emotionally and behaviourally until puberty, which successively predicts offspring depression at the age of 17 [36]. The effects of maternal depression on offspring are parts of the heterogeneous causes of future disorders. Although some of the effects of maternal depression could be prevented or alleviated through certain intervention or therapy, other may affect offspring for their lifetime in various ways.

E. Improvement Through Intervention Programs

Are there any solutions to eliminate or weaken the negative effects of maternal depression? The answer is yes. The study found that prenatal psychotropic medication treatment not only helps with prenatal maternal depressive symptoms but also infant cortisol level after they are born [9]. However, the long-term effects of medication on infant cortisol reactivity are unknown. Medication use during pregnancy should still be considered carefully and more clinically oriented follow-up studies should be conducted. After delivery, negative effects primarily stem from the unengaging interactions between depressed mothers and infants. Interventions on improving maternal communication styles can weaken the negative effects of maternal depressive symptoms. A study by Cicchetti and colleagues in 2000 [4] examined the effect of Toddler-Parent Psychotherapy (TPP), an intervention program aiming to improve the relationship between mothers and infants. As a result of this intervention, the cognitive functioning of infant from depressed group improves to match that of non-depressed group, which suggests that cognitive developmental deficits can be alleviated and prevented by early intervention. Similar evidence from Verduyn and others [5] shows again that child problems and maternal depression can be lessened by early intervention.

III. CONCLUSION

Maternal depression mainly influences offspring's social, language and cognitive development through the characteristics of depression such as low energy and loss of interests. The inactive interaction between mothers and their offspring can result in delays in social, language and cognitive development. Luckily in general these effects may not last for a long time and can be corrected by proper interventions designed to improve the quality of mother-infant interactions. These effects may disappear as offspring associate with other family or friends without depressive symptoms or as their mothers get better. However, prenatal programming effects through elevated cortisol level or altered amygdala connectivity are more likely to have a long-lasting influence, for biological changes are less likely to be reversed. These biological effects may aggravate offspring stress coping and emotional regulation abilities and may increase

their future risk of depression. Motherhood is a challenge physically and mentally. Future studies should investigate the biological mechanisms of the transgenerational influence of maternal depression from mothers to offspring, so that researchers can identify and help mothers with depression early on. Moreover, more sociological studies should be conducted to find ways to improve pregnant women's living environment and remove potential stressors. These efforts will not only help a great number of women, but also ameliorate the negative influences of maternal depression on offspring and the potential generations to come.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

JW did the literature review and wrote the paper.

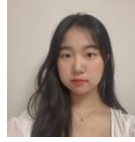
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REFERENCES

- [1] A. Mian, "Depression in pregnancy and the postpartum period: Balancing adverse effects of untreated illness with treatment risks," *Journal of Psychiatric Practice*, vol. 11, no. 6, pp. 389-396, 2005.
- [2] C. Martins and E. A. Gaffan, "Effects of early maternal depression on patterns of infant-mother attachment: A meta-analytic investigation," *The Journal of Child Psychology and Psychiatry and Allied Disciplines*, vol. 41, no. 6, pp. 737-746, 2000.
- [3] D. Cicchetti, F. Rogosch, and S. Toth, "The efficacy of toddler-parent psychotherapy for fostering cognitive development in offspring of depressed mothers," *Journal of Abnormal Child Psychology*, vol. 28, no. 2, pp. 135-148, 2000.
- [4] C. Verduyn, C. Barrowclough, J. Roberts, N. Tarrier, and R. Harrington, "Maternal depression and child behaviour problems: Randomised placebo-controlled trial of a cognitive-behavioural group intervention," *British Journal of Psychiatry*, vol. 183, no. 4, pp. 342-348, 2003.
- [5] S. Sohr-Preston and L. Scaramella, "Implications of timing of maternal depressive symptoms for early cognitive and language development," *Clinical Child and Family Psychology Review*, vol. 9, no. 1, pp. 65-83, 2006.
- [6] A. Qiu *et al.*, "Prenatal maternal depression alters amygdala functional connectivity in 6-month-old infants," *Translational Psychiatry*, vol. 5, no. 2, pp. e508-e508, 2015.
- [7] B. B. Gump, J. Reihman, P. Stewart, E. Lonky, T. Darvill, D. A. Granger, and K. A. Matthews, "Trajectories of maternal depressive symptoms over her child's life span: Relation to adrenocortical, cardiovascular, and emotional functioning in children," *Development and Psychopathology*, vol. 21, no. 1, pp. 207-225, 2009.
- [8] P. Brennan, R. Pargas, E. Walker, P. Green, D. J. Newport, and Z. Stowe, "Maternal depression and infant cortisol: influences of timing, comorbidity and treatment," *Journal of Child Psychology and Psychiatry*, vol. 49, no. 10, pp. 1099-1107, 2008.
- [9] B. R. William, "Children of parents with major affective disorder: a review," *American Journal of Psychiatry*, vol. 140, no. 7, pp. 825-832, 1983.
- [10] J. Cohn, S. Campbell, R. Matias, and J. Hopkins, "Face-to-face interactions of postpartum depressed and nondepressed mother-infant pairs at 2 months," *Developmental Psychology*, vol. 26, no. 1, pp. 15-23, 1990.
- [11] T. Field, "Early interactions between infants and their postpartum depressed mothers," *Infant Behavior and Development*, vol. 7, no. 4, pp. 517-522, 1984.
- [12] T. Field, B. Healy, S. Goldstein, and M. Guthertz, "Behavior-state matching and synchrony in mother-infant interactions of nondepressed versus depressed dyads," *Developmental Psychology*, vol. 26, no. 1, pp. 7-14, 1990.
- [13] S. Orr and C. Miller, "Maternal depressive symptoms and the risk of poor pregnancy outcome," *Epidemiologic Reviews*, vol. 17, no. 1, pp. 165-171, 1995.
- [14] L. Singer, "Maternal psychological distress and parenting stress after the birth of a very low-birth-weight infant," *JAMA*, vol. 281, no. 9, p. 799, 1999.
- [15] L. J. Pawlowski and R. Hansen, "Neurodevelopmental outcome at 8 months and 4 years among infants born full-term small-for-gestational-age," *Journal of Perinatology*, vol. 24, no. 8, pp. 505-514, 2004.
- [16] D. Lawlor, "Intrauterine growth and intelligence within sibling pairs: findings from the mater-University study of pregnancy and its outcomes," *Journal of Epidemiology & Community Health*, vol. 59, no. 4, pp. 279-282, 2005.
- [17] S. Shenkin, J. Starr, and I. Deary, "Birth weight and cognitive ability in childhood: A systematic review," *Psychological Bulletin*, vol. 130, no. 6, pp. 989-1013, 2004.
- [18] M. Weissman, E. Paykel, and G. Klerman, "The depressed woman as a mother," *Social Psychiatry*, vol. 7, no. 2, pp. 98-108, 1972.
- [19] M. Lovejoy, P. Graczyk, E. O'Hare, and G. Neuman, "Maternal depression and parenting behavior," *Clinical Psychology Review*, vol. 20, no. 5, pp. 561-592, 2000.
- [20] D. Cicchetti and S. Toth, "The development of depression in children and adolescents," *American Psychologist*, vol. 53, no. 2, pp. 221-241, 1998.
- [21] D. Cicchetti and S. Toth, "The development of depression in children and adolescents," *American Psychologist*, vol. 53, no. 2, pp. 221-241, 1998.
- [22] P. Kuhl, "Cross-language analysis of phonetic units in language addressed to infants," *Science*, vol. 277, no. 5326, pp. 684-686, 1997.
- [23] C. Snow, "Mothers' speech to children learning language," *Child Development*, vol. 43, no. 2, p. 549, 1972.
- [24] P. Kaplan, J. Bachorowski, and P. Zarlengo-Strouse, "Child-directed speech produced by mothers with symptoms of depression fails to promote associative learning in 4-month-old infants," *Child Development*, vol. 70, no. 3, pp. 560-570, 1999.
- [25] A. Piteo, L. Yelland, and M. Makrides, "Does maternal depression predict developmental outcome in 18-month old infants?" *Early Human Development*, vol. 88, no. 8, pp. 651-655, 2012.
- [26] C. D. Weerth, R. Zijl, and J. Buitelaar, "Development of cortisol circadian rhythm in infancy," *Early Human Development*, vol. 73, no. 1-2, pp. 39-52, 2003.
- [27] M. Diego, T. Field, M. Hernandez-Reif, C. Cullen, S. Schanberg and C. Kuhn, "Prepartum, postpartum, and chronic depression effects on newborns," *Psychiatry: Interpersonal and Biological Processes*, vol. 67, no. 1, pp. 63-80, 2004.
- [28] T. Field *et al.*, "Prenatal paternal depression," *Infant Behavior and Development*, vol. 29, no. 4, pp. 579-583, 2006.
- [29] R. Gitau, A. Cameron, N. Fisk, and V. Glover, "Fetal exposure to maternal cortisol," *The Lancet*, vol. 352, no. 9129, pp. 707-708, 1998.
- [30] S. Azak, R. Murison, T. Wentzel-Larsen, L. Smith, and M. Gunnar, "Maternal depression and infant daytime cortisol," *Developmental Psychobiology*, vol. 55, no. 4, pp. 334-351, 2012.
- [31] A. Zietlow, N. Nonnenmacher, C. Reck, B. Ditzen, and M. Müller, "Emotional stress during pregnancy - Associations with maternal anxiety disorders, infant cortisol reactivity, and mother-child interaction at pre-school age," *Frontiers in Psychology*, vol. 10, 2019.
- [32] C. Buss, E. Davis, B. Shahbaba, J. Pruessner, K. Head, and C. Sandman, "Maternal cortisol over the course of pregnancy and subsequent child amygdala and hippocampus volumes and affective problems," in *Proc. the National Academy of Sciences*, vol. 109, no. 20, 2012.
- [33] N. Malykhin, R. Carter, K. Hegadoren, P. Seres, and N. Coupland, "Fronto-limbic volumetric changes in major depressive disorder," *Journal of Affective Disorders*, vol. 136, no. 3, pp. 1104-1113, 2012.
- [34] S. Lupien *et al.*, "Larger amygdala but no change in hippocampal volume in 10-year-old children exposed to maternal depressive symptomatology since birth," in *Proc. the National Academy of Sciences*, vol. 108, no. 34, pp. 14324-14329, 2011.
- [35] A. Holmes *et al.*, "Individual differences in amygdala-medial prefrontal anatomy link negative affect, impaired social functioning, and polygenic depression risk," *Journal of Neuroscience*, vol. 32, no. 50, pp. 18087-18100, 2012.
- [36] A. Koukounari, A. Stringaris and B. Maughan, "Pathways from maternal depression to young adult offspring depression: an exploratory longitudinal mediation analysis," *International Journal of Methods in Psychiatric Research*, vol. 26, no. 2, p. e1520, 2016.

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