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Immunological and other biological correlates of the impact of antenatal depression on the mother-infant relationship

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A B S T R A C T

Antenatal depression affects up to 20% of pregnancies, yet research has historically focused on postnatal depression and its effects on mothers and their offspring. Studies are now emerging highlighting the impact that depression in pregnancy can also carry on both members of the dyad, including difficulties with psychological, physical, and social functioning. More specifically, researchers have begun to examine whether antenatal depression may lead to difficulties in the developing mother-infant relationship and subsequent infant attachment. While much of the research on this has explored psychosocial mechanisms behind the pathway from antenatal depression to a disrupted relationship in the postpartum, few studies have looked at biological underpinnings of this process. Of the literature that exists, it has been found that mothers with depression in pregnancy have lower levels of oxytocin and increased levels of inflammatory markers, plausibly creating difficulties in the mother-infant bonding process, leading to impaired mother-infant interactions and non-secure infant attachment. Furthermore, infants with non-secure attachments are at risk of entering a proinflammatory state due to a dysregulated stress response system. Overall, the literature on the neurobiology of mother-infant interactions and infant attachment in the context of antenatal depression is sparse, thus warranting future research.

1. Introduction

Major depressive disorder (MDD) during any point of pregnancy, that is, antenatal MDD, can occur both in women with and without a history of depression and affects up to 20% of pregnant women (Biaggi et al., 2016). Antenatal MDD, characterized by low mood, insomnia, and anhedonia, may occur as either a continuation of symptoms that began prior to conception, or as an episode that specifically began during any trimester of the pregnancy, and is diagnosed using the same criteria as an episode of MDD outside of pregnancy. The severity of the depression, e.g. mild, moderate, severe, is determined by the number of symptoms present, the severity of the symptoms, and the functional impairment caused by the symptoms. In addition to antenatal MDD, up to 45% of women may suffer from depressive symptoms throughout pregnancy that do not quite meet clinical criteria for a major depressive episode (Corbani et al., 2017; Josefsson et al., 2001).

While there is not a plethora of research investigating the aetiology of clinical depression and depressive symptoms in pregnancy, it is thought that a combination of social and biological factors may underpin the emergence of symptoms during a period when hormones are already rapidly changing (Sawyer et al., 2018). Notable risk factors include: a history of childhood maltreatment, a history of MDD, socioeconomic difficulties, young age, lower education qualifications, and lack of social support (Leigh and Milgrom, 2008); and, furthermore, biological factors such as hypothalamic-pituitary-adrenal (HPA) axis changes, including altered diurnal cortisol patterns, and elevated biomarkers correlating with systemic inflammation(Nazzari et al., 2020; Osborne et al., 2018). Studies have been mixed as to which trimester poses the greatest risk for depression: some have found that the first trimester has the highest prevalence (Gavin et al., 2005), while others have found that the second and third trimesters have a higher incidence (Bennett et al., 2004). Furthermore, women who experience depression during pregnancy are at heightened risk for the depression to continue into the postnatal period and beyond (Biaggi et al., 2016).

Research has begun to identify that depression in pregnancy can carry long-lasting biological, clinical, and psychosocial implications for not only mothers, but for their babies as well (Madigan et al., 2018; O'Donnell, Glover, Barker, & O'Connor et al., 2014; Pawlby, Hay, Sharp, Waters, & O'Keane, 2009; Van den Bergh et al., 2020), and that these outcomes are not only from women who are clinically depressed, but also those with sub-clinical depressive symptoms. Furthermore, these outcomes can alter infant development through to adulthood. Women depressed in pregnancy (and their babies) are more likely to have alterations in their biological systems, including their HPA axes and immune systems (Osborne et al., 2018), they are more likely to continue to be unwell beyond the antenatal period and are at heightened risk for poor clinical outcomes (Bauer et al., 2014). Additionally, their offspring are more likely to develop psychopathology themselves, especially internalising and externalising disorders (Madigan et al., 2018; Van den Bergh et al., 2020), which can last through adulthood (Plant et al., 2015), and

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they are less likely to feel emotionally and physically supported. One pathway in the intergenerational transmission of psychopathology is the relationship that mothers and their infants develop across the perinatal period, and studies show that mothers with antenatal depression are more likely to experience difficulties interacting with their babies which can lead to long-lasting relationship and attachment difficulties (Bind et al., 2021), and that infants who develop non-secure attachments to their mothers are more likely to develop psychopathology themselves (DeKlyen and Greenberg, 2008). While the mother-infant relationship is certainly not the only mechanism underlying intergenerational transmission of psychopathology, it is still of the utmost importance that women with depressive symptoms in pregnancy be identified and treated, to not only support their own mental health, but also to optimise their relationship with their babies in order to engender better outcomes for both.

This mini-review will explore (i) the association between antenatal depression and the mother-infant relationship, from pregnancy through the postpartum; (ii) the biological correlates of difficulties in the developing relationship; and (iii) biological changes in infants with attachment difficulties.

2. Antenatal depression and the mother-infant relationship

Depressive episodes over the course of a woman's perinatal period is a critical factor in determining risk to her offspring's mental health outcomes (Brennan et al., 2000; Luoma et al., 2001), and a disrupted mother-infant relationship in the perinatal period is a possible mechanism underpinning this risk (Murray et al., 1996). In fact, the perinatal period is the most important stage for the development of this relationship between mother and child (Ainsworth, 1979). While much of the literature on the mother-offspring relationship focuses on attachment, typically examined after the first year of life, equally important are the earliest mother-infant interactions, both in pregnancy and in the early postpartum, as they provide information on the quality of the developing bond, which is predictive of later attachment security (Crittenden, 2003).

2.1. Antenatal depression and foetal attachment

As mentioned above, women who are depressed in pregnancy are at risk of increased stress, which may affect their developing relationship with their offspring. As such, studies have found that women who are depressed during their pregnancies are at risk to have greater difficulty in bonding with their unborn babies (Misri and Kendrick, 2008). For example, women in a non-clinical sample who exhibit heightened depressive symptoms during pregnancy are also more likely to ruminate and excessively worry during their pregnancies, two symptoms of depression that are found to be associated with difficulties with foetal bonding (the act of a mother emotionally connecting with her unborn baby and preparing for motherhood (Mercer, 2004)), as reported on the Maternal Antenatal Attachment Scale (Schmidt et al., 2016). Furthermore, additional studies have found that women who are clinically depressed in pregnancy report reduced maternal-foetal attachment in the second and third trimesters when administered the Maternal Fetal Attachment Scale (McFarland et al., 2011), measured as "a woman's own reflections on pregnancy and motherhood, her enjoyment of pregnancy, excitement about motherhood, and hopefulness for the future." It is thus unsurprising that in both a clinical and community sample, depression, which manifests as withdrawal and unconnectedness, can render a woman unable to connect with, and care for, her foetus. Given that all of the above-listed studies have utilised self-reports when assessing maternal-foetal attachment, it is to be expected that women experiencing depression would subjectively rate their attachment as diminished. Further studies examining the association between antenatal depression and maternal-foetal attachment would benefit from observational methods of assessment to understand whether the link is both subjective and observed.

2.2. Antenatal depression and the mother-infant interaction

It is important to identify difficulties in foetal attachment, as it is a known predictor of maternal sensitivity—that is, the ability for a mother to comfortably engage her infant and adjust her behaviour according to her infant's cues—and the quality of the mother-infant relationship in the postpartum period (Petri et al., 2018), i.e. how attuned a mother is to her infant, how engaged and soothed the infant is by its mother, and how well the dyad come together as a whole. While the literature on this is sparse, it is thought that women who are antenatally depressed and are having difficulties bonding with their unborn baby will be at heightened risk for suboptimal mother-infant interactions postnatally and reduced sensitivity. In fact, observational studies confirm that antenatal depression is associated with observed disruptions in the mother-infant relationship in the postpartum, regardless of presence of postnatal depression (Bind et al., 2021).

In one study, mother-infant interaction was assessed in the context of both antenatal and postnatal depression, in an effort to elucidate whether there was a difference in dyadic interaction based on timing of maternal symptoms (Pearson et al., 2012). The authors found that women who exhibited high levels of depression during mid pregnancy, but not postnatally, were less responsive toward their infants, when observed using the Thorpe Interaction Measure, than women with no antenatal depression. Interestingly, they also found that women who did not experience antenatal depression and who experienced only postnatal depression early in the postpartum, did not have altered responsiveness, but that women whose postnatal depression persisted into the late postpartum did exhibit less responsiveness.

In our recent study (Bind et al., 2021), we found that women (and their babies) who experienced antenatal depression displayed a reduced quality of interaction at both 8 weeks and 12 months postnatal on the Crittenden CARE-Index, highlighting the fact that these changes may be long-lasting across the postnatal period. Furthermore, the difficulties in the interaction were not influenced by postnatal depression, suggesting the mother-infant interaction is affected by antenatal depression independently of postnatal depression, and that postnatal depression only affects the interaction if its occurrence coincides with the timing of the interaction. While neither of the above-listed studies assessed maternal-foetal attachment prior to postnatal dyadic interactions, indeed studies have shown that the association between postnatal depression and less optimal mother-infant interaction may be attributable to a continuation of impaired foetal attachment (that is, in pregnancy) into the postnatal period (Dubber et al., 2015), and that mothers' unresponsiveness may actually begin during pregnancy, not postnatally (Pearson et al., 2012). And furthermore, that foetal attachment has been found to be highly predictive of postnatal bonding (Dubber et al., 2015; Rossen et al., 2016). As the early mother-infant interaction is highly predictive of infant attachment status after 12 months (Crittenden, 2003), and early attachment has long been associated with subsequent offspring outcomes (DeKlyen and Greenberg, 2008), it is thus important to identify mothers at risk of difficulties in their interactions and provide support and guidance.

2.3. Antenatal depression and infant attachment

Given that the mother-infant interaction is an antecedent to infant attachment, some studies have examined whether antenatal depression may lead to difficulties in secure attachment formation. One such study recruited women who had a history of MDD, and thus were more likely to experience MDD antenatally, and followed them from pregnancy through to 12 months postnatal (Hayes et al., 2013). The authors tracked mothers' depressive symptoms throughout pregnancy and the postnatal period, and found that the higher the level of depressive symptoms during pregnancy, the more likely infants were to exhibit disorganized attachment at 12 months. In line with some of the literature on the mother-infant interaction, this effect was completely independent of

postnatal psychopathology, further indicating that mood symptoms during the antenatal period may actually be more linked to attachment disruptions between mother and child than in the postnatal period. Another study that analysed the effect of historical maternal depression (that is, prior to the postnatal period) on infant attachment found that while depressive symptomology was associated with insecure attachments, this effect was seen in women who experienced depression in addition to another psychiatric diagnosis (Carter et al., 2001). These results suggest it may the combination of depression with another psychopathology that contributes to attachment difficulties in infancy.

Finally, one review that analysed the literature on perinatal depression and infant attachment posited that the effects of postnatal depression on the mother-infant interaction and infant attachment may begin in the antenatal period, whereby women who are depressed in pregnancy are more likely to continue to be depressed in the postpartum, and this continual depression will interfere with their abilities to sensitively care-give (Lefkovics et al., 2014). Interestingly, though, the authors hypothesized that if a mother can engage responsively with her infant, this may protect the developing attachment. It has been suggested that depression in isolation may not account for attachment changes, but rather, it may be depression in addition to many other risk factors that are typically comorbid with antenatal depression, including socioeconomic difficulties, lack of social support, interpersonal conflict, and other adversity, that contribute to insecure and disorganized attachment styles (Carter et al., 2001).

3. Biological changes involved in the pathway from antenatal depression to mother-infant relationship and attachment difficulties

The most researched psychosocial factors that contribute to maternal sensitivity and infant attachment security are: maternal emotional availability, maternal comfort and warmth, maternal mentalisation—the ability for a mother to treat her infant as its own mental agent in the context of needs, feelings, thoughts, beliefs, and desires (Meins et al., 2001)—and optimal neonatal behaviour (Grossmann et al., 1985). Conversely, factors that have been found to contribute to impaired interactions and insecure organized attachment styles are: maternal psychopathology (Hipwell et al., 2000), difficult infant temperament (Susman-Stillman et al., 1996), socioeconomic hardship (Spieker and Booth, 1988), maternal history of childhood abuse (Bernier and Meins, 2008), maltreatment of the infant (Carlson et al., 1989), and maternal psychopathology (Hayes et al., 2013). Less researched, though, is the role that maternal biological changes in pregnancy and the postpartum, in conjunction with depression, may have in the development of relationship difficulties.

3.1. Antenatal depression and oxytocin

While many studies have explored the psychosocial underpinnings of the mother-infant relationship development, research has also emerged on the biological antecedents to the attachment process, that is, whether a mother's biological signature may translate to her caregiving behaviours and her infant's attachment. One of the most vital neurohormones involved in the mother-infant bonding process, both in utero and in the postpartum, is oxytocin, which is released during the perinatal period in both mothers and their infants (Sawyer et al., 2018; Trinetti, 2019). More specifically, oxytocin is typically highest in concentration in brain regions associated with attachment behaviours, and is passed from mother to baby via the birthing process and breast milk (Feldman et al., 2007). Furthermore, it triggers maternal caregiving behaviour (Insel and Young, 2001), and thus is vital for maternal sensitivity and attunedness. Studies have shown that mothers with decreased levels of circulating oxytocin during pregnancy have greater difficulty in bonding with their newborns, exhibited through decreased attachment behaviours and preoccupation with the infant (Feldman et al., 2007). Furthermore, reduced oxytocin in the postnatal period is associated with a decrease in maternal sensitivity and overall parenting quality (Kohlhoff et al., 2017), highlighting the importance of oxytocin in the formation of an optimal mother-infant relationship.

Of note, oxytocin is also thought to be a protective factor with regard to mental health (McQuaid et al., 2014). Interestingly, studies do find sex differences in oxytocin's role in depression, such that males tend to have heightened oxytocin when depressed, while females experiencing depression have depleted oxytocin levels (Yuen et al., 2014). Moreover, studies have found that lower levels of circulating oxytocin are associated with an increase in severity of depression (Scantamburlo et al., 2007). And, finally, studies show that, specifically during pregnancy, women with depressive symptoms have decreased oxytocin levels both during pregnancy (Serati et al., 2021) as well as in the postpartum(Eapen et al., 2014), overall highlighting the importance of oxytocin in the perinatal period for maternal mood and stress levels. Furthermore, women who are antenatally depressed are both less likely to initiate (Stark et al., 2018) as well as continue breastfeeding throughout the postpartum (Yusuff et al., 2015). As lactation and breastfeeding are associated with surges of oxytocin in both mother and baby (Moberg and Prime, 2013), it is possible that one reason mothers who were antenatally depressed have diminished circulating oxytocin is because they are less likely to breastfeed their infants.

Interestingly, it has been found that polymorphisms in the oxytocin signalling pathway are associated with both risk for depression in pregnancy and with changes in maternal vocalisations towards infants, which are crucial for sensitive caregiving (Mileva-Seitz et al., 2013). Thus, given that mothers with antenatal depression are less likely to vocalise with their infants in the postpartum (Bind et al., 2021), it is plausible that one biological explanation for why antenatal depression is associated with decreased maternal sensitivity, increased unresponsiveness, and impaired overall quality of the relationship, is due to depression-mediated decreased caregiving in mothers with oxytocin polymorphisms.

3.2. Antenatal depression and inflammation

Of note, research has emerged that oxytocin also plays a vital role in anti-inflammatory processes throughout the body (Szeto et al., 2008), that greater levels of inflammation are associated with reduced oxytocin, and that oxytocin administration can bring down inflammation. The association between reduced oxytocin and heightened inflammation lends credence to recent findings that women with depression in pregnancy have increased circulating inflammatory markers in the late second and early third trimester, including IL-6, IL-10, TNF-α, and CRP (Lahti--Pulkkinen et al., 2020; Osborne et al., 2018) and decreased circulating oxytocin (Garfield et al., 2015), compared with non-depressed women at the same gestational timepoint. Furthermore, studies find that women with histories of maltreatment, a significant risk factor for perinatal depression, are more likely to experience a pro-inflammatory state (Boeck et al., 2016), coupled with reduced oxytocin (Heim et al., 2009). Thus, it is plausible that one mechanism through which an inflamed state can lead to depression, especially in perinatal mothers, is via reduced available oxytocin (Garfield et al., 2016), given oxytocin's protective factors for mental health Furthermore, studies show that inflammation levels tend to be higher in women with untreated depression compared with women whose depression is being managed with medication (Miller et al., 2018), suggesting attenuation of depressive symptoms—and thus a plausible increase in oxytocin—helps to reduce inflammation.

3.3. Antenatal depression and foetal programming

In addition to diminished oxytocin and increased inflammation—-which suggests that difficulties in the mother-infant interaction stem from maternal behavioural alterations due to her own biological changes—it is also possible that antenatal depression may lead to infant attachment problems because of infant behavioural difficulties, driven by foetal programming effects. Researchers have proposed that foetal programming, whereby an infant's stress regulatory system develops in

utero, is impacted by mothers' stress during pregnancy, biomarkers (including glucocorticoids and inflammatory markers) of which have been found to be elevated during depression (O'Connor et al., 2014; Osborne et al., 2018; Seth et al., 2016).

In other words, one theory posits that antenatal depression is associated with elevated circulating maternal cortisol, and given that cortisol can cross the placental barrier, and that there are many glucocorticoid receptors in the placenta, it will pass into the developing foetus and impact foetal development and stress regulation (Sarkar et al., 2008). In fact, it is thought that maternal antenatal depression may be one precursor to infant difficult temperament based on animal studies which show that offspring exposed to stress in utero display behavioural difficulties, increased HPA axis activity in response to stress, and heightened fear responses (O'Donnell and Meaney, 2017; Weinstock, 2008), all predictors of subsequent difficulties in mother-infant interactions. Furthermore, offspring of mothers with antenatal depression are found to have greater amygdala connectivity (Qiu et al., 2015), a finding that may help to explain infants' heightened fearfulness and stress reactivity given the amygdala's role in fear response. Studies have shown that infants exhibiting heightened fear and stress experience have greater difficulty in the mother-infant relationship (Duschinsky, 2018), lending credence to the idea that heightened maternal glucocorticoid output in pregnancy may induce neurodevelopmental changes in foetal brains, which in turn affects infant stress reactivity and thus their ability to self-regulate and interact.

In addition to elevated cortisol, more recent studies have hypothesized that foetal programming effects on infants may also occur via heightened maternal inflammation (Nazzari and Frigerio, 2020; Rakers et al., 2020). As mentioned above, women with antenatal depression are more prone to elevated inflammation in pregnancy, and recent studies have found associations between maternal antenatal depression, increased inflammatory markers, and disrupted infant neurodevelopmental outcomes, including behavioural regulation (Osborne et al., 2018)—an identified precursor of later mother-infant interactive abilities (Greene et al., 1983). The association between maternal inflammation and infant developmental and behavioural changes may be due to neuroanatomical differences that occur when a developing foetus is exposed to inflammation (Graham et al., 2018); more specifically, infants exposed to in-utero inflammation are more likely to have greater amygdala volume and connectivity, a similar finding to studies examining the effect of cortisol on neurodevelopment.

Moreover, studies have identified that psychiatric problems during pregnancy are associated with altered foetal behaviour, possibly due to sympathetic nervous system activation (Monk et al., 2011). In a recent systematic review, Van den Bergh et al. (2020) found that infants who were exposed to depression and stress in utero were more likely to display alterations in their autonomic nervous system functioning in the postpartum. Of note, other studies have suggested that the effects of maternal depression on infant attachment difficulties may be mediated by autonomic nervous system alterations, mainly, disrupted stress reactivity. Furthermore, it is thought that foetal programming may actually occur not only in-utero, but also extend to the early postnatal period as well; thus, effects of maternal stress in-utero may continue to exert influence over the development of the infant postnatally, when the mother-infant attachment is forming (Bergman, Sarkar, Glover, & O'connor, 2008).

Thus, with a dysregulated neuroregulatory system, infants are more likely to have trouble forming attachments to their mothers (Hayes et al., 2013). More specifically, studies have found that infants with difficulties regulating themselves are more likely to form insecure and disorganized attachments to their mothers (Hayes et al., 2013), which may be due to the fact that elevated maternal glucocorticoids in pregnancy pass on to infants, thereby affecting their abilities of stress and emotion regulation as well as their neurodevelopment—all key components to optimal relationship and attachment formation. In fact, studies have shown that neonates of mothers who were depressed in pregnancy have difficult behaviour and disrupted self-regulatory abilities (Osborne et al., 2018), and given that neonatal behaviour is found to be predictive of how the mother-infant relationship will develop (Bind et al., 2021), it is plausible that there is a pathway through which depression-related biological changes in mothers may translate to difficult infant temperament and subsequent disrupted interactions and attachment (see Fig. 1).

4. Biological effects of attachment difficulties in infants

Due to the fact that maternal antenatal depression-driven biological alterations, such as increased inflammation and stress hormones and decreased oxytocin, can translate into difficulties in the mother-infant relationship, it is also important to understand whether difficulties in the infant's developing attachment may in turn translate to subsequent biological changes. In a recent study, Measelle et al. (2017) found that infants with non-secure attachment styles to their mothers, that is, insecure or disorganized, had higher levels of salivary C-reactive protein (CRP) than infants who were securely attached, with the highest inflammation in infants who were disorganized. Given that attachment security is necessary for developing infants to cope with stressors, without a secure attachment and an internal working model for stability and adequate stress reactivity, ongoing dysregulation and distress (two classic markers of a disorganized infant), are likely to increase an infant's susceptibility to inflammation and lead to biological changes. The authors also found that mothers of infants with greater CRP were more likely to have been depressed—an unsurprising finding given that patients with depression have heightened CRP levels (Pitharouli et al., 2021)—again highlighting the interplay between maternal psychopathology, inflammation, and mother-infant relationship difficulties.

As discussed above, infants of mothers with antenatal depression are more likely to develop a disorganized attachment (Hayes et al., 2013), and thus a pathway may exist whereby a mother who is depressed in pregnancy provides inadequate or insensitive care to her infant in the postpartum due to her own presence of psychopathology and biological changes, her infant subsequently develops a disorganized attachment style in response, and this disrupted attachment is associated with a proinflammatory state due to a hyperactive stress response. Studies show that adversity in the early years is a risk factor for later psychopathology and disease (Plant et al., 2013), and given that adversity is highly associated with inflammation (Danese et al., 2007), these results suggest that there may be a connection between heightened neurobiological activity in infants due to attachment problems and future health and wellbeing difficulties.

Furthermore, studies have found that infants with insecure or disorganized attachment styles experience higher levels of circulating cortisol in response to stress than securely-attached infants (Bernard and Dozier, 2010; Spangler and Grossmann, 1993). This finding is to be expected given that non-secure attachments are associated with decreased maternal sensitivity and atypical or unpredictable behaviour (Lyons-Ruth, Bronfman and Parsons, 1999), and, furthermore, that decreased maternal sensitivity has been linked to greater stress reactivity and cortisol output in infants due to a lack of predictable reassurance in the face of stress (Blair et al., 2006; Gunnar et al., 1996). One mechanism thought to underlie this association is that infants who do not receive consistent and sensitive caregiving must escalate, and dysregulate, their behaviour to achieve a response from their caregiver, thus hyperactivating their neuroendocrine systems (Hertsgaard et al., 1995). Or, alternatively, in response to not receiving sensitive and responsive caregiving, infants become increasingly stressed and cortisol will rise. Other studies on attachment disorganization, however, show that disorganized infants actually experience a blunting of cortisol rather than an overactivation (Luijk et al., 2010). Given that attachment disorganization may stem from ongoing fear of, or neglect by, a caregiver, it is possible that over time, continual maltreatment may dampen cortisol reactivity in some infants due to chronic physiological dysregulation.

5. Limitations and conclusions

Overall, there is evidence to suggest that one mechanism underpinning the relationship between maternal antenatal depression and

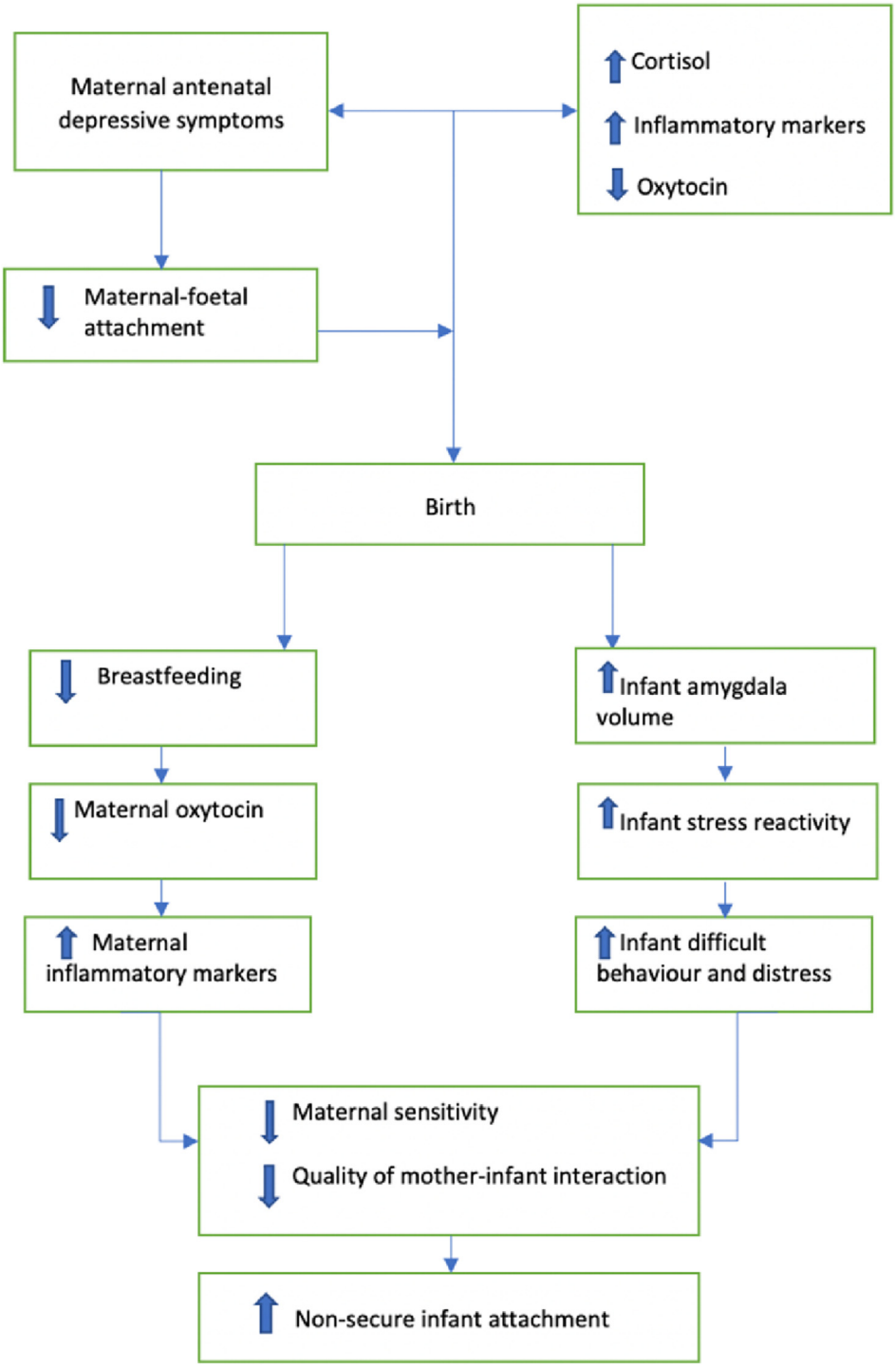

Fig. 1. Biological correlates linking antenatal depression to mother-infant relationship difficulties.

difficulties in the mother-infant relationship and subsequent infant attachment may be biological alterations in both mother and baby. For example, studies find that women who are depressed in pregnancy are more likely to have alterations in their HPA axes and inflammatory markers, leading to greater cortisol and inflammation, both of which are shown to pass through the placental barrier and impact foetal neurodevelopment(Osborne et al., 2018). Moreover, women with antenatal depression are found to have lower circulating oxytocin, a hormone that is inversely associated with inflammation, suggesting that there is a relationship between depressive symptoms, increased inflammation, and decreased oxytocin (Serati et al., 2021). As oxytocin is the major hormone involved in mother-infant bonding and interactive abilities (Sawyer et al., 2018), it is unsurprising that depleted oxytocin would be associated with early bonding difficulties.

In addition to the association between maternal depression, biological changes, and sub-optimal mother-infant interaction, there also appears to be a link between infant attachment difficulties and biological changes in infants. For example, studies find that infants of mothers who were depressed in pregnancy are more likely to display non-secure attachment styles (Hayes et al., 2013), and furthermore, that there is an association between insecure and disorganized attachments and increased inflammation in infancy (Measelle et al., 2017). While it is

difficult to disentangle which comes first between inflammation or a non-secure attachment, it is unsurprising that infants with non-secure attachments would exhibit heightened inflammation, given the lack of security and stability they experience.

As the overall literature on the topic of biological correlates of the mother-infant interaction in women who experience depression is sparce, it warrants further research, as studies have long shown the effects of intergenerational transmission of psychopathology not only affects offspring mental health, but also biology and predisposition to disease (Plant et al., 2015). Furthermore, there are many established pathways linking antenatal depression to altered outcomes in children, and difficulties in the mother-infant relationship is just one such mechanism. While research has begun to disentangle the differential effects of the antenatal environment from the postnatal environment on mother-infant outcomes (Bind et al., 2021; Osborne et al., 2018; Pearson et al., 2012), future research would benefit from specific exploration of whether depression during each timepoint has a differing effect, or whether both time points work in conjunction with each other to disrupt the mother-infant relationship and infant biological outcomes.

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Declaration of competing interest

None.

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