Perinatal depression effects: A narrative review

Tiffany Field*

Abstract
This narrative review summarizes publications from the last eight years (2010-2018) on the early interactions, developmental effects and physiological and biochemical profiles of perinatally depressed mothers and their infants. Depressed mothers are nonresponsive with their infants. The depressed mothers' physiological profiles including low vagal activity, right frontal EEG activation and fMRI activation differences are consistent with the mothers' lack of responsivity during interactions with their infants. Biomarkers of the mothers that would affect their mood states include elevated cortisol as well as low serotonin, dopamine and oxytocin levels. The infants of depressed mothers come to early interactions with a prenatal history of growth delays and less responsivity to fetal stimulation. At birth they have physiological and biochemical profiles that are similar to those of their mothers. They continue to show these profiles in later development (e.g. depressed vagal activity and elevated cortisol). Although their later behavior problems and cognitive delays have been attributed to the depressed mothers’ lack of responsivity during early interactions, these problems may also relate to their own lingering physiological and biochemical profiles.

Keywords: Perinatally depression, Biomarkers

Introduction
The Diagnostic and Statistical Manual of Mental Disorders (DSM-5) does not distinguish prenatal from postpartum depression [1]. Rather, it is called perinatal depression (peripartum episodes) even though as many as 40% of women have their first episode of depression later in the postpartum period [2]. Postpartum depression continues to affect some 10-15% of women [3,4]. Among the women in a study on 2,252 pregnancies and postpartum periods, 5% had episodes during pregnancy and 30% during the postpartum period [5]. In a more recent study on 111 women, depression at 24 hours postpartum was the only significant predictor of postpartum depression at four months, contributing to 29% of the variance [6]. Although postpartum depression effects have continued to be attributed to the mothers’ lack of responsivity during early interactions with their infants, research has more recently focused on the physiological and biochemical profiles of perinatal depression. The infants’ profiles that are similar to those of their mothers suggest that the infants’ own neurobiology further impacts their development. This may reflect intergenerational, in utero and/or birth trauma factors. The profiles also highlight the need for more transactional research that assesses the interactive effects of the mother and infant variables.

Aim Of This Review
The aim of this narrative review was to summarize research on perinatal depression that was published over the last eight years (2010-2018) to critique that research and to suggest further directions. The narrative review was intended to be comprehensive rather than selective to provide...
readers a cross-section of the research on this topic.

**Methods**

For this review, literature searches were conducted on PubMed and PsycINFO using the terms perinatal, prenatal and postpartum depression. Inclusion criteria were studies, reviews and meta-analyses from the last eight years on perinatal depression. Exclusion criteria were animal research, case studies and non-English publications. The literature search yielded 146 papers, but following exclusion and inclusion criteria, 64 were rejected, leaving 82 papers for the final review. Earlier studies have also been cited here as supporting material for the more recent literature. Although the search was limited to the terms perinatal, prenatal and postpartum depression, several topics emerged including mother–infant interactions, mediators of those interactions, longer-term developmental effects, and physiological and biochemical profiles of the mothers and the infants. This review is accordingly divided into sections on those topics. Limitations of the research and future directions are suggested throughout.

**Results**

**Mother-Infant Interactions**

Depressed mother–infant interactions have frequently been studied in face-to-face conditions including the still–face procedure and the double video protocol. In the still–face procedure, the mother is interacting with her infant and suddenly holds her face still while continuing to look at her infant and the infant shows gaze aversion and negative affect [7].

**Still-face interactions**

Using the still-face paradigm, infants of depressed versus non-depressed mothers displayed less negative affect during the still-face phase at 5 months, suggesting that the infants had become accustomed to their mothers’ flat affect [8]. Using the same paradigm, another research group reported that the behavior of depressed mothers and infants during the still–face was bidirectional as opposed to being mother-driven or infant-driven [9].

**Double video interactions**

In the double video procedure, the infant interacts face-to-face with the mother via a closed–circuit computer system [10]. A spontaneous interaction is followed by a replay of the mother from the spontaneous interaction such that the mother’s behavior is no longer contingent on the infant’s behavior. This paradigm features five interaction phases including a live interaction followed by a replay followed by a second live interaction followed by a replay followed by a third live interaction. In one study on this paradigm, the infants of depressed mothers showed continuous gazing at the mother independent of the type of interaction and showed no difference in their affect across the interactions, suggesting that the infants had become accustomed to their mothers’ non-contingent behavior [11]. In contrast, the infants of non-depressed mothers showed more looking and positive affect during the live, contingent interactions. The depression diagnosis in this study was unfortunately based on the self-report Edinburgh Postnatal Depression Scale [12], making it difficult to compare to earlier studies that had used the same paradigm but with clinically depressed mothers [13,14]. In addition, the mothers’ behaviors were not reported [11]. This research group subsequently reported the behaviors of the depressed mothers from the same database [15]. They noted that the depressed mothers showed the same amount of positive and negative affect independent of the quality of their interactions with their infants. Reporting the infants’ and the mothers’ data in separate papers makes it difficult to determine the synchrony or the reciprocity between the mothers’ and infants’ behaviors.

**Touch as a mediating/moderating variable during mother-infant interactions**

Touch synchrony during mother-infant interactions has been noted to moderate the effects of postpartum depression on infant self-regulation in at least one study [16]. In this paradigm, nine-month-old infants were exposed to four different conditions including anger with mother, anger with stranger, joy with mother and joy with stranger. Gaze and touch synchrony were less frequent for the depressed versus the non-depressed mothers, although touch synchrony appeared to moderate
the negative effects of maternal depression on the infants' behavior.

Another example of touch being a mediating variable comes from one of the few spontaneous interaction studies in the recent literature on postpartum depression [17]. In that study, 26 depressed mothers and 44 nondepressed mothers and their four-month-old infants engaged in 10-minute interactions. The interactions were coded for three types of touching including caregiving, affectionate and static touch based on the Maternal Touch Scale [18]. Caregiving touch was associated with sensitive behavior for both the depressed and nondepressed mothers. Surprisingly, that association was the same for both groups of mothers. The same research group conducted sequential analyses to compare caregiving versus playful maternal touch [19]. When the infants were showing negative affect, the mothers were more likely to initiate caregiving touch. Again, surprisingly, only the postpartum depressed mothers initiated affectionate touch when their infants were showing negative affect. In contrast, others have reported less affectionate touching by postpartum depressed mothers [20] and more negative touching by depressed mothers [18].

Infant temperament as a mediating variable during mother-infant interactions

Infant temperament has been another mediating variable for the responsivity of postpartum depressed mothers during early interactions with their infants. Infants of depressed mothers have been noted to have more difficult temperament including lower scores on rhythmicity, persistency and amenability and higher scores on activity [21]. Positive emotionality in the infants has been related to greater responsivity of the mothers (N=102) [22]. In another study on 203 mothers and their infants, negative temperament in the infants mediated the negative effects of the mothers' depressive behaviors on their interactions [23]. These studies were limited by the use of self-report as opposed to observational measures and by their cross-sectional and correlational nature. However, the mediating relationship of infant temperament has also been noted in an observational study on mother-infant interactions in a sample of 167 dyads [24]. In this study, infant negativity at 4 months mediated the relationship between maternal depression at four months and maternal sensitivity during mother-infant interactions at 15 months. It is not clear why only infant behaviors were coded at 4 months and only mother behaviors were coded at 15 months even though the interactions were videotaped at both time periods.

Limitations

Several limitations can be noted about this literature on depressed mother-infant interactions. These include the absence of systematic reviews and meta-analyses which relates to the variability on several dimensions across studies. The studies vary by the infants being different ages and by a wide age range (3-18 months) across studies and even within studies. For example, 9-14-month-old infants were included in one study because as the authors suggested, “This age range was chosen because the mother-infant relationship emerges reliably during this period” [23]. Nine to fourteen months would be considered a non-optimal age for studying face-to-face interactions inasmuch as face-to-face is a primary form of interaction until infants are crawling and playing with toys at which time toy play interactions become more salient. The variability in the types of interactions across ages would also argue against averaging interaction ratings across ages as was done in one study on 6, 12 and 18-month-old infants [25]. This is also problematic given that 79% of mothers are reputedly no longer depressed by 13 months [26].

Some of the researchers sampled clinically diagnosed depressed mothers [13] while others have relied on self-report depression scales for identifying the mothers [12]. And, they have typically not controlled for antidepressant use or therapy [27]. The studies have also varied on their interaction situations including spontaneous, still-face, double video and mother-stranger anger-joy conditions, some of which are distressing for both the mother and infant [9]. And, the coding systems for these have varied from global ratings to micro-analytic coding [19].

Despite these methodological limitations, many of the research groups attribute the longer-term developmental effects to the mothers’ depressed behaviors during these early interactions. For
example, at the conclusion of a depressed mother-infant interaction study, the data were referred to as the “cross-generational transfer of emotional maladjustment from depressed mothers to their infants” [16]. And, in the introduction to a UK longitudinal study on depressed mother-infant interactions, the authors say “Given the importance of maternal responsiveness for infant development, the association between depression and reduced maternal responsiveness may partly explain why infants of depressed mothers are more likely to show insecure attachment and behavioral, emotional and cognitive disturbances as they grow up” [28]. These attributions are perhaps not surprising, as many of the longer-term developmental effects have been noted in longitudinal studies that start with maternal depression effects on mother-infant interactions during the first six months.

**Developmental Effects**

Developmental effects of perinatal depression have been noted in children as old as 8 years in the recent literature. Many of these have been reported in longitudinal studies that started as early as six weeks postpartum and show an impact on infants’ communication skills, imitation, cognitive development, physical growth and psychological problems.

**Communication skills**

Communication skills were assessed at 12 and 24 months in a study that classified mothers as depressed on the Edinburgh Postnatal Depression Scale (EPDS) at six weeks (N=1555) [29]. The mothers’ depression at four months was correlated with lower levels of communication skills at both 12 and 24 months. These findings are limited by their reliance on maternal self-report for both perinatal depression and infant communication skills.

**Imitation**

Imitation at 13 months has been related to postpartum depression in a longitudinal study on British infants (N=253) [30]. In this study, postpartum depression was determined at six months based on a clinical interview, and the assessment of imitation involved the infants imitating modeled actions. The infants of depressed mothers showed a 72% reduction in the likelihood of imitating the modeled actions.

**Cognitive development**

Infants' cognitive development has also been negatively affected by maternal perinatal depression. In a longitudinal study on Danish infants (N=83, N=29 depressed), maternal depression was determined by a diagnostic interview at four months postpartum, and the infants’ cognitive development was assessed by the Bayley Scales of Infant and Toddler Development at four and 13 months [26]. The mothers’ depression was associated with inferior cognitive development at four months but not at 13 months. The absence of effects at 13 months may relate to 79% of the mothers no longer being depressed at 13 months [26]. When maternal depression has persisted across 18 months, infants’ cognitive scores have remained lower than those of infants of non-depressed mothers [31]. And, in a meta-analysis of seven studies that included 974 children two years of age and older, the children of postpartum depressed mothers had lower full-scale IQ scores [32].

**Physical growth delays**

Physical growth delays have also been attributed to postpartum depression effects [33]. In this systematic review based on 20 articles that met criteria, growth during the first year was most affected. Children of depressed mothers had a greater likelihood of being underweight and growth delayed. Unfortunately, a pooled effect could not be estimated due to the variability of the databases.

**Psychological problems**

Children's psychological problems as late as eight years have been associated with postpartum depression [34]. In this study, both postpartum depression assessed by the EPDS at two, three and six months post-delivery and current mental health problems had independent and additive effects on children’s psychological problems based on the Child Behavior Checklist.

**Limitations**

These developmental effects reported in the recent literature on perinatal depression have frequently been attributed to the mothers' depressed
behaviors during their early mother-infant interactions. However, these effects are confounded by several variables. These include the time of onset and the duration of the mothers' depression. The very few longitudinal studies suggest a continuity of maternal depression from pregnancy to the postpartum period [35] and across at least 13 months of the postpartum period for at least 21% of depressed mothers [26]. Other confounds are the mothers' physiological and biochemical profiles that have been studied prenatally and post-natally but not longitudinally. Further, the infants' physiological and biochemical profiles that are similar to the mothers' profiles at least at the neonatal stage [36] would contribute to these developmental effects, although they are also lacking longitudinal research.

**Depressed Mothers' Biochemical Profiles**

Depressed mothers have differed from non-depressed mothers on their biochemical profiles including several hormones and neurotransmitters. The recent literature has focused on cortisol, oxytocin, serotonin, tryptophan and even vitamin D. The word "profiles" is perhaps a misnomer given that multiple hormones and neurotransmitters are not typically assayed in the same study, although they are known to be related. For example, tryptophan is a precursor of serotonin [37] and oxytocin has been noted to suppress cortisol [38]. It's not clear why saliva samples are not assayed simultaneously for both oxytocin and cortisol as saliva assay technology is available for both cortisol and oxytocin.

**Cortisol and alpha amylase**

HPA axis dysfunction has been most frequently reported for perinatal depression including hypersecretion of cortisol and abnormal diurnal secretion [39-44]. High, flat levels of cortisol have been noted during pregnancy and postpartum [45,46]. In one study, hair cortisol levels predicted 22% of the variance in postpartum depression symptoms [40]. In a systematic review on 199 studies including 151, 651 pregnant women, HPA dysregulation was the strongest predictor of postpartum depression [44]. A related stress hormone, salivary alpha-amylase, has also been elevated in women with depressive symptoms [47].

**Oxytocin**

Low levels of oxytocin have also been frequently reported for perinatal depression [48,49]. In longitudinal studies, pregnancy oxytocin levels predicted postpartum depression [50,51]. Oxytocin has been related to maternal sensitivity [52,53] and to breastfeeding [54] inasmuch as it is stimulated by sucking, and low levels have been related to early cessation of breastfeeding [55]. Other hormones have been implicated in earlier studies including estradiol, progesterone, brain-derived neurotrophic factor and oxytocin. However, in a study on 549 postpartum depressed women and 968 nondepressed women at 6 weeks postpartum, the depressed and nondepressed groups did not differ on any hormones [56]. This result was surprising but may relate to the statistical problems of unequal sample sizes.

**Serotonin and tryptophan**

The neurotransmitter, serotonin, has been notably low in postpartum depression [57]. This may relate to low levels of tryptophan as a precursor of serotonin [37]. Low tryptophan levels may, in turn, derive from increased stress hormones and pro-inflammatory activity that drives tryptophan.

**Pro-inflammatory markers**

Several pro-inflammatory markers have been elevated prenatally including C-reactive protein [58,59], IL-6 and TNF-alpha [58-60]. Elevated prenatal pro-inflammatory cytokines may, in turn, contribute to low serotonin levels postpartum. Prenatal profiles of elevated cortisol and low levels of the serotonin metabolite SHIAA have been noted to persist into the postpartum period [36].

**Low Vitamin D levels**

Low levels of vitamin D have been related to depressive symptoms both in prenatal and postpartum depression [61]. Negative correlations between vitamin D levels and EPDS or Center for Epidemiological Studies-Depression (CES-D) scores have been reported frequently but mostly for depressed pregnant women as opposed to postpartum depressed mothers [62-65]. In a recent systematic review, 14 of 239 studies met inclusion criteria with a quality assessment ranging from moderate to high [61]. Of the studies on prenatal
depression, 71% showed a significant relationship between prenatal depression and low vitamin D levels. Of the studies on postpartum depression, 55% showed a significant association between depression and low vitamin D levels. Once again, a meta-analysis could not be conducted to determine an overall effect size because the effect estimates and statistical analyses were highly variable across studies.

Limitations
One of the limitations of this biomarker research is the assays of single measures rather than assaying the samples for multiple related measures. For example, cortisol and oxytocin have been noted to have reciprocal effects [27]. Yet, they have been typically assayed alone in studies on perinatal depression even though the same samples could have been assayed for both measures [27]. Multiple measures, i.e. hormones and neurotransmitters, might suggest profiles that would be better predictors than single measures. If, for example, elevated cortisol is coupled with low serotonin, that profile might have more predictive validity than elevated cortisol alone.

Systematic reviews and meta-analyses have been difficult to conduct on this biomarker research because of the heterogeneity of samples and measures. Perinatal depression has been studied at different times during pregnancy and the postpartum period. It has been variously measured by interview and self-report measures and the biomarkers have been assayed in different samples (e.g. saliva versus plasma) at different times of day.

Depressed Mothers’ Neurophysiological Profiles
Several studies in the recent literature on perinatally depressed women have examined functional connectivity in resting states and during emotional conditions using fMRI paradigms. Several of these studies have revealed reduced connectivity in emotion regulation circuits of the brain in the depressed mothers [66]. In an overview of 11 studies conducted on 100 postpartum depressed women, the fMRI findings were similar to those recorded for individuals with major depression [67]. Fiorelli et al suggested that a distinct neurobiological profile could not be determined because of the small sample sizes and the lack of direct comparisons between those with postpartum depression and major depression.

Connectivity during resting states
A couple fMRI studies taken during resting states suggest attenuated connectivity in emotion regulation circuits in postpartum depressed women. In one of these, posterior cingulate cortex (PCC) time series were extracted from the fMRIs of 14 postpartum depressed women and 23 nondepressed women [68]. PCC-right amygdala connectivity was attenuated and that connectivity was positively correlated with PCC-parahippocampus connectivity. Chase et al suggested that postpartum depression might involve the disruption of activity in the regions that regulate empathy. In a similar study, a sample of 32 postpartum depressed women and nondepressed women were examined using fMRIs of the anterior cingulate cortex (ACC), the bilateral amygdala (AMYG), the hippocampi (HIPP) and the dorsolateral prefrontal cortices (DLPFCs) [69]. The postpartum depressed women had attenuated connectivity for all of those regions (ACC, AMYG, HIPP, DLPFC). In addition, attenuated connectivity was noted between corticocortical and corticolimbic regions for the postpartum depressed women. Deligiannidis et al implied that these were tentative findings by calling this a preliminary study.

Connectivity during emotional conditions
Attenuated connectivity has also been noted in the depressed mothers’ fMRIs during emotional conditions, specifically the viewing of photos of their infants. In one study, the mothers viewed and rated four different sets of face photos including positive and negative faces of their own infant and positive and negative faces of an unfamiliar infant [70]. The mothers with higher scores on the EPDS showed reduced amygdala responses to their own infants’ faces versus the unfamiliar infants’ faces. Barrett et al concluded that amygdala function related to their own infants’ faces may be an important factor in mood and in “quality of mothering”. The same group of researchers subsequently published data on postpartum depressed mothers’ fMRI responses to photos of smiling infants (own and other) and positive non-infant photos [71]. The postpartum depressed
mothers as compared to the non-depressed mothers showed decreased bilateral amygdala–right insular cortex connectivity when they viewed their own versus other infants. Wonch et al. suggested that these results represented deficits in the “processing of socially and emotionally relevant stimuli”.

A different research group suggested that they were the first to examine neural responses to infants' emotional faces [72]. The mothers were shown photos of their own and unfamiliar infants’ joyful and distress faces. The depressed mothers showed attenuated responses to their own infants’ distress faces in the dorsal anterior cingulate cortex. Their responses to their own infants’ joyful faces were also attenuated in the orbitofrontal cortex and insula. Laurent & Ablow reported depressed mothers’ fMRI responses to their own versus unfamiliar infants’ (18-month-old) cry sounds [73]. The depressed versus non-depressed mothers failed to show activation of paralimbic and prefrontal regions. The authors concluded that “disturbance of these neural networks involved in emotional response and regulation may help to explain parenting deficits in depressed mothers”.

Disturbances in neural networks involving attenuated connectivity have been attributed in part to activation of neuroinflammatory pathways [74,75] during major depressive episodes. And, as already noted, several pro-inflammatory markers have been elevated prenatally including C-reactive protein [58,59], IL-6 and TNF-alpha [58-60]. Neuronal loss has also been noted during depression [75] but not specifically during perinatal depression.

Limitations
This literature on the neurophysiological responses of perinatally depressed women has several limitations. First, although some researchers in this field have intimated that perinatal depression is similar to non-perinatal depression and others have suggested that perinatal depression has its own characteristics, no direct comparisons have been made to formulate a unique neurobiological profile.

Second, most of the neurophysiological studies that have appeared in the recent literature on perinatal depression have monitored fMRIs. Some have conducted fMRIs during the resting state [68,69] and some during emotional conditions [70,71]. Comparisons between resting states and emotional conditions might have been more informative. Further, the emotional conditions have featured infant faces in static photos which are less representative of interaction stimuli, i.e. moving faces. Videos of infant faces might be more valid stimuli. The studies have also varied by depression measures at different pregnancy and postpartum periods and the connectivity has been measured in different regions. Variability on all of these factors has limited the use of systematic reviews and meta-analyses.

The recent research on neurophysiological markers of perinatal depression has been almost exclusively fMRI research and only on the mothers given that infants are too active for fMRI recording. This has limited any measure of similar patterns across mothers and infants. In earlier studies, both mothers and infants were monitored for heart rate which showed shared rhythms. [76]. Similarly, measures of vagal activity and EEG in both mothers and infants revealed similar profiles of low vagal activity and greater right frontal EEG [77]. Those were notably seen in perinatally depressed mothers and their newborns.

Fetal/Infant Biomarkers Related to Perinatal Depression

Prenatal depression has been implicated in negative effects on fetal and infant development including excessive fetal activity, fetal growth delays, neonatal physiological and biochemical profiles that are similar to prenatal maternal profiles, and continuing effects into later infancy [27]. Although most of these data come from earlier studies, they highlight the need for further research on fetal/infant biomarkers related to maternal depression and whether these persist over development.

Fetal activity and growth delays
Excessive activity has been noted in the fetuses of prenatally depressed women [78]. This may, in turn, affect the lower weight noted in fetuses of prenatally depressed women, [27]. Lower weight has also been attributed to elevated cortisol in the prenatally depressed women [79]. The mothers' elevated cortisol has been thought to both “re-program the infant’s HPA axis and change
developmental trajectories” much as it has in animal studies [80]. Elevated prenatal cortisol and excessive fetal activity may also contribute to the growth delays noted in head circumference, abdominal circumference, length and biparietal diameter [81,27].

Prenatal maternal and newborn cortisol levels
Prenatal cortisol has also been associated with newborn cortisol levels [36]. In this study on 70 depressed and 70 non-depressed women, prenatal cortisol levels of the depressed mothers and their newborns were higher than those of the non-depressed mothers and newborns. In a structural equations analysis, the elevated prenatal maternal cortisol was a significant predictor of prematurity and the elevated prenatal maternal norepinephrine was a significant predictor of low birth weight. And, those infants of prenatally depressed mothers continued to show elevated cortisol at 3 and 6 months [82].

Maternal and infant cortisol levels
Maternal cortisol levels have also been associated with infant cortisol levels and difficult infant temperament including irritability [83,84]. This association has been attributed to the infants’ exposure to the mothers’ milk given that formula-fed infants did not experience these effects [45]. Others have found these associations only in mothers with comorbid depression and anxiety. For example, when a group of mothers with comorbid depression and anxiety was compared to a group with depression only and a non-depressed group, the infants of mothers with comorbid depression and anxiety had higher daytime and bedtime cortisol levels at 6 and 12 months but not at 18 months [39]. Still other comorbidities have interacted with perinatal depression and anxiety including anger [85]. Any of these mood states or any combination of them would likely contribute to elevated perinatal maternal cortisol, although those comparisons have not been made.

Concordance of mothers’ and preschool children’s cortisol levels
The persistence of the concordance of cortisol levels in depressed mothers and infants has not been assessed, although at least two studies have shown concordance of mothers’ and preschool children’s cortisol levels. In one study, the concordance was noted between both average cortisol levels and cortisol fluctuations across the day [86]. And, greater concordance was shown for parents with chronic depression and children with negative temperament as well as children with positive temperament. The latter finding is difficult to interpret, although frequent cortisol sampling and laboratory assessments of temperament lend credence to these findings. In another study, cortisol was sampled twice per day upon awakening and 30 minutes later in 47 working mothers and their preschool age children [87]. Mothers’ cortisol levels were higher than the children’s and cortisol attunement (concordance of the mothers’ and children’s levels) was only noted on non-workdays.

Prenatal maternal and newborn neurotransmitter profiles
Neurotransmitter profiles of newborns have also been similar to depressed mothers’ prenatal profiles including elevated norepinephrine and low levels of serotonin and dopamine [36,27]. Longitudinal studies have not been conducted on infant neurotransmitter profiles to assess the effects of these neurotransmitter profiles or their persistence across infancy. Some have theorized that elevated norepinephrine may contribute to intrauterine artery resistance in fetuses and, in turn, to growth delays due to the slowed transport of nutrients by the intrauterine artery resistance [88]. Fetal ultrasound has confirmed greater intrauterine artery resistance in fetuses of prenatally depressed mothers suggesting this may be a factor in the growth delays noted [81]. Unfortunately, norepinephrine in the mothers and growth delays in the fetuses were not measured in the uterine artery resistance study [88].

Prenatal maternal and newborn vagal activity
Similar prenatal maternal and neonatal physiological profiles might also be considered as biomarkers for newborns and infants of perinatally depressed mothers. For example, vagal activity has been lower in prenatally depressed women and their neonates [36]. Unfortunately, no replication or follow-up studies on infant vagal activity could be found in the current literature on perinatal depression.
Right frontal EEG in mothers, newborns and infants

Right frontal EEG has frequently been noted in prenatally depressed women and their offspring from the neonatal period through infancy and into early childhood, but most of these studies come from earlier years. In these studies, prenatally depressed women and their newborns had greater relative right frontal EEG activation than non-depressed women and their newborns [36], and prenatal depression was a predictor of right frontal EEG activation in both the newborns and postpartum mothers [36]. Prenatal depression has also been a predictor of right frontal EEG activation in older infants [89]. In the Field and Diego study, positive asymmetry values indicated greater relative right frontal activation. The same sample of infants continued to show right frontal EEG at one week, at one month and at three months [90] and again at six months [91].

In the only recent study on EEG and frontal connectivity, infants were seen at 6, 18 and 24 months [92]. Greater right frontal EEG activation in six-month-old infants was associated with increasing maternal depressive symptoms from the prenatal to the postnatal period. This association was not apparent at 18 months, although at that time, increasing maternal depressive symptoms predicted lower right frontal connectivity. And prenatal and early postnatal maternal depressive symptoms were predictive of internalizing and externalizing behaviors of the infants at 24 months. Surprisingly, these findings were noted in the full sample and the female sample but not the males. Soe et al suggested that this phenomenon “may reflect a neural basis for the familial transmission of phenotypes associated with mood disorders, particularly in girls”.

Although most of the right frontal EEG activation noted in infants of depressed mothers has been based on baseline recordings, some investigators have recorded EEG in parallel with viewing faces expressing different emotions as well as during mother – infant play interactions [93]. At three years, children born to prenatally depressed mothers continued to have right frontal EEG [94]. In this study, the preschool children were exposed to a simulated maternal distress condition of the mother feigning being hurt and to another condition of infant cry sounds. The children showed non-empathetic behaviors like hitting their mothers.

Limitations

Prenatal transmission of the mothers’ cortisol and norepinephrine noted in the earlier literature has not been assessed in this recent literature. Although elevated norepinephrine can increase intrauterine artery resistance which would affect fetal growth, norepinephrine levels and fetal growth were not measured in the intrauterine resistance study [88]. The neurotransmitter, cortisol, vagal activity and EEG profiles noted for the depressed pregnant women and their newborns in the earlier literature have not yet been replicated. No comparable multivariate studies have appeared in the recent literature. Only one recent longitudinal study supported the earlier findings on stability of infant EEG across infancy [95]. Unfortunately, no longitudinal replication studies on stability of depressed infants’ cortisol, neurotransmitter or vagal activity biomarkers have appeared in this recent literature.

Limitations of this narrative review and further research

This narrative review is limited to publications from the last eight years (2010-2018) on the early interactions, developmental effects and physiological and biochemical profiles of perinatally depressed mothers and their infants. Several limitations of this literature have been noted including that perinatal depression was typically based on self-report. In addition, it was usually labelled prenatal or postnatal depression depending on when it was measured, although the effects on the offspring could have related to continuing depression over both the prenatal and postnatal periods. Although physiological profiles have been documented for the prenatal and neonatal periods, those have not been assessed after the neonatal period. Longitudinal studies are needed to determine whether those profiles continue across development. In addition to replication studies, multivariate studies are needed to determine relationships between variables. Further, systematic reviews and meta-analysis studies are missing from this literature likely
because the studies have been highly variable on their assessments.

Nonetheless, this literature suggests that depressed mothers’ physiological profiles including low vagal activity, right frontal EEG activation and fMRI activation differences are consistent with the mothers’ lack of responsivity during interactions with their infants. Biomarkers of the mothers that would affect their mood states include elevated cortisol as well as low serotonin, dopamine and oxytocin levels. The infants of depressed mothers come to their early interactions with a prenatal history of growth delays and less responsivity to fetal stimulation. At birth they have physiological and biochemical profiles that are similar to those of their mothers. They continue to show some of these in later development (e.g. depressed vagal activity and elevated cortisol). Although their behavior problems and cognitive delays have been attributed to the depressed mothers’ lack of responsivity during early interactions, the infants’ problems and delays may also relate to their own neurobiology that continues to impact their development. Further research is needed to determine the relative contributions of these variables to later development and to further inform early interventions.

References


Tiffany Field. OAJournal of Pregnancy and Child Care (2018) 1:1


82. Field T, Diego M, Hernandez-Reif M (2009) Depressed mothers' infants are less responsive to faces and voices. Infant Behavior & Development 32: 239-244.


