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Maternal Affective Illness in the Perinatal Period and Child Development: Findings on Developmental Timing, Mechanisms, and Intervention

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Abstract Maternal mental illness is one of the most reliable risks for clinically significant child adjustment difficulties. The research literature in this area is very large and broad and dates back decades. In this review, we consider recent research findings on maternal mental illness and child development by focusing particularly on affective illness the perinatal period. We do this because maternal affective illness in the perinatal period is common; recent evidence suggests that pre- and postpartum maternal depression may have lasting effects on child behavioral and somatic health; research in the perinatal period raises acute and compelling questions about mechanisms of transmission and effect; and perinatal-focused interventions may offer distinct advantages for benefitting mother and child and gaining insights into developmental mechanisms. Throughout the review, we attend to the increasing integration of psychological and biological models and the trans-disciplinary approach now required for clinical investigation.

Keywords Perinatal · Mood disorder · Developmental programming · Child development

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Introduction

Numerous reviews [1] make clear that the association between maternal mental illness and child development is robust across research design and sampling variation; maternal mental illness is reliably associated with child psychopathology but also social functioning and relationship quality, cognitive function, and other aspects of behavioral and somatic health; maternal mental illness is not randomly distributed in the population, and so explanations for its effects are confounded by co-occurring risks such as family conflict and socio-economic disadvantage; maternal mental illness is associated with wide variability in children's adjustment, likely attributable to co-occurring risks and variability in child vulnerability. In other words, whether or not maternal mental illness is associated with child outcomes is no longer in doubt. What defines current research is a focus on the mechanisms involved and the specific implications and translations of the research findings. In this review, we address the role of timing of the child's exposure to maternal affective illness and what it implies for understanding developmental mechanisms and intervention approaches. We focus particularly on affective illness in the perinatal period because it is research on this developmental period that provides some of the more consequential findings for understanding mechanisms and shaping interventions.

Research on postnatal maternal mental illness—depression has attracted the lion's share of the attention—and child health

has been an active area of study for decades [2, 3] and has established postpartum depression as one of the most systematically studied early risks for child development. More recent research findings indicate that the postnatal emphasis needs to be complemented with a prenatal focus. The possibility that child health and disease may be partly but importantly explained by prenatal exposures is gaining considerable influence from several lines of study. The model underlying this work is generally referred to as developmental or fetal programming [4], which proposes that the developing fetus adapts to exposures *in utero*, perhaps because the fetus may be especially susceptible to exposures and/or adaptations to exposures during this early period may confer benefit to the organism, e.g., by forecasting something about the nature of postnatal exposures. Fetal adaptations that result from fetal or developmental programming are thought to have evolutionary value; there is abundant evidence that this process is conserved across species [5••].

Brief Background on Maternal Affective Illness and Symptoms in the Perinatal Period

Affective illness in the perinatal period is common. The prevalence rate of 13 % in the postpartum period, based on a meta-analyses of some years ago [6], has been generally supported in more recent studies, which also indicate elevated rates of depression in anxiety in the perinatal period [7]. Quite what accounts for affective illness in the perinatal period and whether it has particular (i.e., distinct from non-perinatal period) causes has attracted considerable attention. Research findings indicate that the risks associated with depression in the perinatal period match those associated with depression outside the perinatal period, e.g., [8], although there is some evidence from experimental and genetic studies to suggest a particular role of estrogen receptors, for example [9, 10••].

Particularly valuable are those studies that seek to identify possible causes of maternal affective illness in pregnancy that might also account for adverse effects on the child; results of these studies will have an impact on understanding mechanisms and devising (preventive) interventions. Among many possible targets in this line of research, obesity has attracted substantial recent interest because of its rising prevalence and gained knowledge about the role that obesity may play in the biology of inflammation and depression. For example, as in non-pregnant women, obesity is associated with higher rates of depression and anxiety in pregnancy and the postpartum period [11]; additionally, obesity, like affective illness, is linked with a range of pregnancy and obstetric complications [12, 13] and effects on the child, including metabolic and neurodevelopmental problems [14, 15]. Managing obesity in pregnancy could therefore have multiple beneficial effects—on the mother, the health of the pregnancy and obstetric outcome, and the child's neurodevelopment. This is one of an increasing number of examples of the need for greater focus on timing of interventions and broader consideration of psycho-biological processes that expand beyond a singular mechanistic or disciplinary territory.

Just as there are several plausible risk factors for maternal mental health, such as obesity, there are several mechanisms through which they may shape perinatal and child health. Stress physiology (particularly involving the HPA axis), autonomic nervous system, and more recently, immunology/inflammation are targets for clinical research because of a growing evidence base supporting their role in affective illness in the perinatal period; evidence that both systems undergo normative change in the course of a healthy pregnancy; and mounting evidence that both types of mechanisms have plausible roles in the early somatic and neurobehavioral development of the child (these processes are considered below).

Developmental Timing of Exposures and Effects

A fundamental question for clinical research is when in development the effects of maternal affective illness may be detectable in the child, and if there are particular periods of ontogenetic vulnerability. A program of study of Murray and colleagues suggests that exposure to maternal postnatal depression may be one example [16•]. Findings on postpartum depression have been among the most influential in discussions of early sensitive periods [17]. However, not all studies support that conclusion, as in the case of a large Canadian cohort assessing emotional disorder [18] or the case of a large German cohort investigating cognitive development [19]. There are indeed multiple sources of variability in child development associated with maternal affective illness, and these will confound studies of timing. And, it is important to note that virtually none of the studies could experimentally control for timing of exposure to maternal depression when drawing conclusions about developmental timing.

One important piece of evidence informing concepts of developmental timing and lists of candidate mechanisms is the observation that there are reliable associations between maternal affective symptoms and child development from the fetal period. Some of the earliest support for an association between maternal psychological experiences and fetal functioning emerged in data demonstrating women's acute emotional reactions affecting the fetus. In 1967, obstetricians Copher and Huber [20] told the third trimester pregnant women that they were breathing air that "contained only half the amount of oxygen necessary to support fetal life… [though their] normal body mechanisms would probably compensate" (p. 323). This "psychogenetic stimulation" produced

immediate increases in maternal and fetal heart rate (FHR). Since then, a relatively systematic approach to neurobehavioral assessment before birth has emerged that focuses on FHR, FHR variability (FHRV), fetal movement (FM), and coupling (the correlation between FM and FHR changes). There is now reliable evidence that inducing maternal stress as well as relaxation alters FM and FHRV, e.g., [21]. More specifically, self-reports of high maternal stress are associated with lower levels of the second and third trimester FHRV and coupling [22]; anxiety associates with more overall activity [23]; and depression associates with more FM in mid gestation [24]. Additionally, a laboratory-induced stress paradigm at 36–38 gestational weeks was associated with a coincident elevation in FHR for fetuses whose mothers were high on self-report anxiety, as well as those who reached diagnostic criteria for depression and/or co-morbid depression and anxiety, e.g., [25]. Associations between women's chronic mood states and late-stage fetal behavior indicate that throughout pregnancy, fetal neurobehavior is shaped by experience-associated alterations in women's biology through adaption to repeated activation patterns (stress, relaxation, exercise) and/or the direct influence of species-atypical variation in maternal biological homeostasis and regulation evidenced in affective symptomatology.

Predictions from fetal behavior to early childhood are noteworthy and highlight the value of predicting fetal behavior. For example, FHRV is positively associated with cognitive and motor abilities at age of 2 years old [26], and greater coupling with more mature neural integration at birth based on assessments using brain stem auditory evoked potential [27]. Fetal behavior has also been linked with infant temperament reactivity [28]. Studies of fetal behavior help substantiate the putative *in utero* fetal programming process. Although no study has linked fetal behavior to long-term developmental outcomes, there is growing suspicion—captured by the fetal programming hypothesis—that the fetal period may define a period of particular ontogenetic vulnerability (see below).

Developmental Mechanisms of Transmission and Mediators of Child Outcomes

How it is that maternal affective illness may shape the somatic and behavioral health of the child has commanded research attention for decades. A variety of alternative mechanisms have been proposed; differentiating among these is important for improving prevention and intervention. A first distinction that is required is whether or not the transmission from maternal affective illness to child adjustment is psychosocially mediated. To date, much of the research attends to compromised parental sensitivity and increased family conflict that co-occur with, and may be secondary to, maternal affective illness and could explain its effect on the child [1]. Similarly, maternal affective illness co-occurs with, and may be secondary to, the rich array of psychosocial adversities that attend mental illness, from poor economic opportunities to exposures to major life adversities. Leverage for distinguishing among these confounded explanations is typically inadequate in studies reported to date, but there is overwhelming correlational evidence of the relevance of these and related factors. And, of course, there are many mechanisms of transmission that may not be directly psychosocial or environmental in nature. Genetics is an obvious one. It is now widely appreciated that children of parents with an affective illness may themselves develop mental disorder because of a shared genetic risk, even if the genetic mechanism or target is not specified.

Appreciation of the role that prenatal maternal affective disorder may have in shaping child health and development raises a separate set of mechanistic questions and candidates. That is, if there are prenatal programming influences associated with maternal affective illness for child outcomes, then there must also be a further class of mechanisms that involves neither psychosocial exposure nor genetic transmission (although it is plausible and even likely that these kinds of risks compel each other for child disorder to result). The maternal ANS/cardiovascular and HPA axis systems are two primary biological effectors of emotion experiences that are potential mediators affecting fetal neurodevelopment with potentially lasting effects into childhood. Research on the fetus has identified associations between CRH in the third trimester and diminished habituation in the FHR response and overall greater arousal [29]; and higher third trimester cortisol and higher systolic blood pressure with higher overall FHR [30]. And, although until recently largely ignored, maternal affective symptoms may alter placenta function in a way that moderates fetal exposure to glucocorticoids [31•].

Studies showing that prenatal maternal anxiety (or, in some studies stress or depression) predicts persisting psychopathology in the child/adolescent [32, 33] are significant for implying a robust prediction that is congruent with fetal programming effect. However, the obvious and important follow-up questions of how maternal anxiety is communicated to the fetus and what in the fetus/child may be "programmed" to account for persisting effects have not yet been answered. Predictably, much of the attention is on stress physiology and the programming of the fetal/child HPA axis, but evidence of this is limited in scope and effect size [34], and it is not yet clear that this is one mechanism accounting for the observed effects on neurodevelopmental and psychiatric outcomes. Changes in child immune system from prenatal maternal anxiety have also been reported, e.g., [35] and may account for somatic and neurodevelopmental outcomes—although, that too has yet to be confirmed. Finally, recent evidence of genetic moderation of the prenatal programming effects on child psychopathology, e.g., [36] is notable for implicating further

mechanisms, such as catecholamines and BDNF. What is clear from the above discussion is that questions about timing of exposure raise corresponding questions about mechanisms of effect, and the list of plausible and supported mechanisms is now long enough to pre-empt singular explanations, silver bullet molecules, or overly focused neurocircuits.

Intervention

To identify an intervention for maternal affective illness to benefit the child is to make assumptions about the mechanisms involved (what needs to be altered?) and the role of timing (when shall it be delivered?). Here again, it is valuable to consider interventions starting from the prenatal period. As noted, prenatal manipulations of maternal mood, for example, by relaxation, may influence fetal behavior [21]. Exercise manipulations may also work, with one study showing effects on FHR [37]. The evidence base for prenatal interventions for maternal anxiety, depression, or stress is still limited [38], but future studies aiming to reduce maternal prenatal distress may yield efficient and practical benefits that could also offer unprecedented leverage for testing developmental programming hypotheses. Alterations of maternal mood, exercise, and diet all warrant investigation if the aim is to improve maternal, perinatal, and child health.

In contrast, sound empirical research on interventions to prevent and reduce maternal postnatal depression is fairly well developed. An early review of interventions to prevent postnatal depression yielded largely disappointing results [39] but a more recent review of 28 randomized controlled trials was considerably more sanguine in its conclusion, particularly concerning the impact of individualized, telephone-based lay support, interpersonal psychotherapy (IPT), and professional-based home visits [40]. It may be premature to declare the list of evidence-based programs; however, specific studies and reviews [41] identify other potential clinical approaches, such as cognitive-behavioral therapy.

One significant task for perinatal-focused interventions for maternal psychological distress is to examine if the beneficial effects on the mother promote the health of the child. The available research is not yet encouraging. For example, in the latter Dennis review [40], there was no overall beneficial effect on infant development or key care measures (immunization, child abuse), but this component was included in only a small number of trials. Nonetheless, other studies have reported that reducing postpartum depression is not adequate for improving the child-parent relationship [42]. And, a review of research including the perinatal period and beyond [43] suggested that improving maternal depression does not readily benefit the child, particularly for independent assessments of the child (which are clearly more compelling than mother-reported outcomes). The implication is that improving child development will require more than merely reducing maternal depression. That implies, indirectly, that mechanisms other than those directly linked with maternal mood may be at play, and it is consistent with limited work showing that postnatal and prenatal factors combine in predicting child developmental outcomes [44].

Conclusion

Recent research findings on maternal mental illness and child development reviewed above have expanded the developmental periods requiring intensive research focus, the list of mechanisms of effect, and the intervention options that might promote maternal and child health. Equally importantly, the program of research seeking to uncover why maternal mental illness shapes child development offers several general lessons for clinical research, including the conjoint consideration of developmental timing and mechanisms of action; the multiply determined nature of child health outcomes and the consequent difficulty in disentangling causal processes; and the multidisciplinary nature of effective contemporary clinical research. These broader lessons about research strategy are valuable because they are a necessary fining tool for interpreting specific findings from individual studies and because they generalize to other clinical-developmental topics in human health and development.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no competing interests.

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