[Archived] Commentary on Dr Janet DiPietro's Article, "Prenatal/Perinatal Stress and Its Impact on Psychosocial Child Development"

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Introduction

Janet DiPietro's article is an integral part of a larger research effort to shed light on the basic developmental principles of early life. Current research is exploring the role of observed, complex, dynamic, bidirectional gene–environment interplay in shaping structural and functional development in early life (ie, epigenetic development), along with the implications of this interplay on mental and physical health over a lifespan. DiPietro began her empirical work by examining biobehavioural development processes in newborns and preterm infants,[1,2] and went on to study these and related processes in the human foetus. DiPietro is now an internationally recognized leader in the field of child development. Her published work has described for the first time the ontogeny of human foetal brain–behaviour relations throughout gestation,[3,4,5]

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associations of maternal and foetal characteristics with the neurobehavioural maturation of the foetus,[7,8] and the foetal neurobehavioural origins of individual differences in infant physiology[8] and behaviour.[9]

Research and Conclusions

DiPietro states that there is mounting evidence to support the notions that maternal psychosocial stress during pregnancy influences birth outcomes regarding length of gestation and foetal growth; that the effects of maternal stress on these birth outcomes is modest in magnitude; that maternal stress may directly influence the developing foetal nervous system; that these effects on brain development may be exacerbated over time by various characteristics of the postnatal developmental trajectory; and that existing research on the effects of maternal prenatal/perinatal stress on child development lacks conceptual and methodological consistency and scientific rigor.

Each of the above assertions is well supported by findings in the empirical literature to date. Although most methodologically rigorous studies now support the conclusion that human maternal psychosocial stress plays a significant role in adverse birth outcomes, some major questions have yet to be addressed, namely: 1) What is the magnitude of the effect of maternal psychosocial stress on various birth outcomes and related constructs? 2) Do the effects of maternal psychosocial stress on outcome(s) vary according to the type or dimension of stress (eg, objective vs subjective stress)? 3) Are the effects of maternal psychosocial stress on outcome(s) modulated by the time or the stage of gestation during which the stress occurs (ie, during critical periods of vulnerability)? 4) To what extent are the effects of stress moderated by other factors such as medical risk, behavioural risk, and sociodemographic characteristics?; and 5) What are the biological and behavioural mechanisms that mediate the effects of psychosocial stress on foetal/neonatal/infant developmental outcome(s)?

With reference to the magnitude of stress-related effect sizes, our review of empirical literature from 1990 to 2001 suggests that preterm births or foetal growth restrictions were twice as prevalent in pregnant women who reported high levels of stress as in women reporting low levels of stress. The magnitude of the effects of psychosocial stress is comparable to that of most other *established* obstetric risk factors, such as medical complications in pregnancy or high-risk behaviours. On one hand, these findings certainly support the argument that maternal psychosocial processes during pregnancy are at least as important and warrant the same degree

of consideration and study as other *established* obstetric risk factors. On the other hand, as pointed out by DiPietro, the magnitude of the effect sizes is small to modest. A doubled risk of premature delivery implies that of all the pregnant women in a high-stress category, 20% may deliver a premature infant, as opposed to 10% of all pregnant women who are not in a high-stress category. Thus, 80% of high-stress-category women deliver within standard gestational parameters. While this finding is encouraging in itself, we must ascertain with greater specificity and sensitivity which of the particular women reporting high psychosocial stress levels during pregnancy are at increased risk for adverse outcomes. DiPietro emphasizes that defining and measuring psychosocial stress is a complicated undertaking because the effects of stress are not only a function of exposure to potentially stressful circumstances but also of an individual's subjective appraisal of the stress in her life. Such appraisals may, in turn, be modulated by other factors. Our review of the literature suggests that studies reporting significant effects using *subjective* measures of stress on birth outcomes greatly outnumber studies using *objective* measures of these constructs, thus underscoring the importance of accuracy and precision in the measurement of subjective states and affect. Without exception, every published human study of maternal stress in pregnancy relies on self-report measures based on a retrospective recall of psychological state and affect over time. It is well recognized that self-report, summary measures of subjective states are highly susceptible to numerous, systematic biases that adversely impact accuracy (eg, the effects of recency, maximum saliency, and valence of affect at the time of recall/reporting[10]). Given the unsatisfactory measurement of psychosocial stress in behavioural perinatology research, it is difficult to ascertain whether the modest effect sizes observed in this body of literature are a function of truly weak or small effects, or rather of some deficiency in measurement procedures.

Animal models and observed changes in physiological responses to exogenous challenges during human gestation suggest there may be critical periods of vulnerability with respect to the effects of maternal psychosocial stress.[11,12,13] Nonetheless, very few human studies have incorporated multiple assessments, especially during the first trimester, which may be the most crucial period. Based on our review of the literature on human studies, when examined by trimester of assessment, a greater proportion of studies report a more significant effect for a first trimester assessment of stress than for a second or third trimester assessment. Moreover, proportionally fewer studies averaged stress scores across trimesters and found a significant stress effect than studies that did not collapse or average scores across trimesters but looked at the separate effects of each assessment. Taken together, these findings support the argument that the stage

of gestation may modulate the effects of maternal stress on foetal developmental outcomes.

DiPietro points out that there are no direct neural connections between the maternal and foetal compartments, and that the effects of maternal psychosocial processes may be mediated via endocrine and vascular mechanisms. It is probable that, in addition to these pathways, maternal–placental–foetal immune processes may also play an important role in mediating the effects of maternal psychosocial stress on foetal developmental outcomes.[12]

DiPietro suggests that development problems in childhood may have their origins in stress-related birth outcomes (such as preterm birth and foetal growth restrictions) or may be a direct consequence of stress effects on developing foetal brain systems. She concludes that because the effect of maternal stress on birth outcomes (eg, length of gestation, foetal growth) is small in magnitude, it may not portend serious developmental effects. However, given the probability that maternal stress influences biological processes related to foetal growth, parturition *and* brain development (the same physiological systems that mediate growth and parturition play a critical role in various aspects of brain development) and the likelihood that measurement problems in the assessment of maternal stress make it difficult to ascertain the true magnitude of stress effects on birth outcomes, this particular conclusion may be somewhat premature.

Implications for the Policy and Services Perspective

As DiPietro points out, given the paucity of empirical data, it is difficult to formulate specific policy implications. Although the literature on animal studies strongly supports a causal role for maternal prenatal stress in a range of adverse developmental outcomes, there are major differences in reproductive physiology across various species, and even across primates, that make it very difficult to generalize findings from animals to humans; in fact, the *only* known animal model in reproductive physiology that approximates human reproductive physiology is that of the gorilla.[14] But in humans, we must begin by assessing the construct of maternal psychosocial stress with greater accuracy. Then, based on empirical evidence, we must ascertain which particular women are reporting high levels of stress, their circumstances, and gestational period to determine when the these women and their foetus may be especially vulnerable to the deleterious effects of stress. I would contend that these data must be well established before specific policy recommendations can be made. Others may argue that broad-based intervention programs be promulgated, using the rationale that some reduction in adverse outcomes is better than no reduction (ie, better than not having any intervention programs at all). However, there is

a drawback to formulating and promoting broad policies for stress reduction. As DiPietro points out, stress does not always act as a developmental teratogen (ie, the extent of harm is proportional to the degree of stress exposure). Indeed, a certain degree of stimulation and activation may be beneficial or even necessary for optimal foetal development. The unqualified notion that all stress during pregnancy is harmful to a foetus may also prompt a certain degree of anxiety and self-blame in women. Ironically, this reaction may spiral in some women, who may be unable to change their circumstances (because they need to work to support the family, for example) and may lead to more subjective stress as they contemplate their stressful lives. Without first determining who needs assistance and how it might be most effectively provided, intervention programs may have a *null* effect (similar to the observed null results of across-the-board antimicrobial therapy for pregnant women with reproductive tract infections[15]).

With the above considerations in mind, we strongly endorse DiPietro's position that public policy to govern the behaviour or activities of pregnant women (with a view to improving developmental outcomes in children) not be forged—for the time being. But, in the same breath, we would add that further empirical research is needed in this critical area as our goal would be, precisely, to develop a more informed set of public policies to promote the health and well-being of children from intrauterine 'life' onward.

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