Psychological adversity in pregnancy: what works to improve outcomes?


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Psychological adversity in pregnancy: what works to improve outcomes?
Vivette Glover and Jane Barlow

Abstract

**Purpose** – Foetal programming is one of the key mechanisms by which physical and social adversity is biologically embedded during pregnancy. While early interest in such programming focused on the long-term impact of the mother’s nutritional state on the child’s later physical health, more recent research has identified an increased risk of psychopathology in children of women who have experienced stress, anxiety and depression during pregnancy. The purpose of this paper is to examine the literature addressing the impact of stress in pregnancy and the implications for practice.

**Design/methodology/approach** – An overview of the literature has been provided.

**Findings** – Both anxiety and depression in pregnancy are common, with a prevalence in the region of 20 per cent. Exposure in pregnancy to anxiety, depression and stress from a range of sources (e.g. bereavement, relationship problems, external disasters and war), is associated with a range of physical (e.g. congenital malformations, reduced birthweight and gestational age), neurodevelopmental, cognitive, and emotional and behavioural (e.g. ADHD, conduct disorder) problems. The magnitude is significant, with the attributable risk of childhood behaviour problems due to prenatal stress being between 10 and 15 per cent, and the variance in cognitive development due to prenatal stress being around 17 per cent. A range of methods of intervening are effective in improving both maternal anxiety and depression, and in the longer term should improve outcomes for the infant and child.

**Research limitations/implications** – This research highlights the importance of intervening to support the psychological wellbeing of pregnant women to improve outcomes for infants and children, and points to the need for further research into innovative ways of working, particularly with high-risk groups of pregnant women.

**Keywords** – Interventions, Stress, Depression, Anxiety, Prenatal, Foetus, Reflective Function

Introduction

The phenomenon of foetal programming, which refers to changes in the environment in utero during specific critical periods and the consequential long-term effect on the child, has until recently focused on the consequences of the mother’s physical health (mostly her nutritional state) in terms of the vulnerability of the child to cardiovascular and related diseases (Barker, 1991, 2003). More recent research, however, has highlighted the role of the mother’s psychological wellbeing during pregnancy (e.g. stress) in terms not only of the physical development of the foetus (e.g. birthweight for gestational age, earlier delivery and pregnancy induced hypertension) (Cardwell, 2013), and physical outcomes, such as an increased risk of asthma (Khashan et al., 2012), but also later psychopathology. For example, there is now considerable evidence from prospective studies that the children of women who are depressed, anxious or stressed during pregnancy are more likely to experience a range of adverse neurodevelopmental, emotional, behavioural, and cognitive outcomes compared with children of mothers who do not experience such problems (e.g. Van den Bergh et

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In the first part of this overview of the literature we examine the research highlighting the ways in which a number of aspects of maternal psychological functioning during pregnancy, focusing specifically on stress, anxiety and depression, can adversely impact on the foetus/infant and later development of the child. This section will also examine the impact of other aspects of psychological functioning in pregnancy such as maternal reflective function. The second part of the paper examines a number of evidence-based methods of working to support women during pregnancy to improve outcomes for both mother and infant.

Maternal mental health in pregnancy

The prevalence of depression in the antenatal period is similar to postpartum levels and ranges from 12 to 20 per cent (Marcus et al., 2003). Antenatal anxiety is also common, with as many as 21.9 per cent of women experiencing anxiety in pregnancy (Heron et al., 2004). Both anxiety and depression in pregnancy are associated with postnatal depression (Heron et al., 2004).

Many women also experience other problems in pregnancy that are strongly associated with both anxiety and depression. For example, around 30 per cent of domestic abuse starts during pregnancy (Department of Health, 2010), and around 9 per cent of women are being abused during pregnancy or after giving birth (Taft, 2002). Around 1 per cent of pregnancies in the UK (20,000 women per year) involve a drug dependant mother (Home Office, 2003), and such drug dependency co-exists with a range of other problems including psychiatric disorder (Frischer et al., 2005) and psychopathology (Hans et al., 1999), particularly disorders of affect regulation (Taylor et al., 1997).

Types of psychological functioning associated with altered child outcome

A wide range of psychological exposures have been associated with altered child outcomes and can all be subsumed under the generic term “stress”. This is a complex term, which can be defined in terms of physiological responses such as activation of the cortisol producing hypothalamic-putitary-adrenal axis, but is here used to cover a range of maternal experiences. Those that have been shown to be associated with altered child outcome vary from very severe stress, such as that caused by the death of an older child, to quite mild stresses, such as caused by daily hassles. They include symptoms of maternal anxiety (O’Connor et al., 2002; Austin, 2004; Obel et al., 2003; Mennes et al., 2006; McMahon et al., 2013), and depression (O’Connor et al., 2002; Pawlby et al., 2011), pregnancy-specific anxiety and daily hassles (Huizink et al., 2003), bereavement (Khashan et al., 2008) and stress due to a relationship problems with the partner (Bergman et al., 2007). They also include exposure to acute external disasters (Laplante et al., 2008), 9/11(Yehuda et al., 2005), Chernobyl (Huizink et al., 2008) a Louisiana hurricane (Kinney et al., 2008), and war (van Os and Selten, 1998).

Impact of adverse mental health

Adverse prenatal mental health has been shown to be associated with a wide range of outcomes both in the short (i.e. immediately following birth) and longer term (i.e. through to adolescence and adulthood). Very severe stress in the first trimester such as the death of an older child has been shown to be associated with an increase in congenital malformations (Hansen et al., 2000), while less severe forms of stress is associated with somewhat lower birthweight and reduced gestational age (Rice et al., 2010; Wadhwa et al., 1993); and

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an altered sex ratio, with fewer males to females being born than in an unstressed population (Obel et al., 2007; Peterka et al., 2004).

A number of studies have also identified an impact on neurodevelopmental functioning of newborns (e.g. functioning on the Neontal Behavioural Assessment Scale, Diego et al., 2004); and psychopathological outcomes of infants and toddlers (e.g. difficult temperament; Austin et al., 2005; Buitelaar et al., 2003, sleep problems; O’Connor et al., 2007), and lower cognitive performance and increased fearfulness (Bergman et al., 2007).

Studies that have examined the association between prenatal stress and neurodevelopmental outcomes in children age three to 16 years, show an increased risk of child emotional problems, especially anxiety and depression, and symptoms of ADHD and conduct disorder (O’Connor et al., 2002, 2003; Kleinhaus et al., 2013; Rice et al., 2010; Van Den Bergh and Marcoen, 2004; Rodriguez and Bohlin, 2005; Beversdorf et al., 2005). Other studies have shown a reduction in cognitive performance (Laplante et al., 2008; Mennes et al., 2006) associated with prenatal stress.

Some studies have found an association between prenatal stress in mid to late gestation and increased risk of autism (Kinney et al., 2008; Beversdorf et al., 2005) although a large population study has failed to confirm this finding (Li et al., 2009). Two studies have found an increased risk of schizophrenia in adults born to mothers who experienced stress during pregnancy. Both showed associations with severe stress (i.e. the death of a relative, Khashan et al., 2008, and exposure to the invasion of the Netherlands in 1940 (van Os and Selten, 1998) during the first trimester.

A further set of studies have shown associations between prenatal stress and a range of altered physical and physiological outcomes. These include specific regional reductions in brain grey matter density (Buss et al., 2010), which may be associated with neurodevelopmental and psychiatric disorders as well as cognitive and intellectual impairment. Several studies have shown that prenatal stress is associated with an altered diurnal pattern or altered function of the HPA axis, although the pattern of alteration is quite complex (Glover et al., 2010).

There is little consistency in the literature regarding the most sensitive time in gestation for the influence of prenatal stress, and it is likely that there are different times of sensitivity dependent on the outcome studied, and the stage of development of the relevant brain or other structures. The two studies of schizophrenia (Khashan et al., 2008; van Os and Selten, 1998), for example, found the most sensitive period was in the first trimester, which is when neuronal cells are migrating to their eventual site in the brain, a process previously suggested to be disrupted in schizophrenia. In contrast two studies of conduct disorder, or antisocial behaviour, found the greatest associations with stress in later pregnancy (Rice et al., 2010; O’Connor et al., 2003).

Recent research has also begun to identify the importance of other aspects of psychological functioning in pregnancy (the impact of which appears to be transmitted via the mothers parenting postnatally rather than biologically or physically during pregnancy) such as the mother’s capacity for reflective functioning (RF). RF in pregnancy is defined as the mother’s imagined relationship with her baby (Slade and Patterson, 2005). Women who are described as “Balanced”, for example, can provide “richly detailed, coherent stories about

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their experiences of their pregnancies and their positive and negative thoughts and feelings about their fetuses”. Women who are “Disengaged”, however, appear to be uninterested in the foetus per se or their relationship with it, and demonstrate “few thoughts about the babies” future traits and behaviours or themselves as mothers; women described as “Distorted” tend to be “tangential or express intrusive thoughts about their own experiences as children, often viewing their foetuses primarily as an extension of themselves or their partners” (Levendosky et al., 2011, p. 214).

The importance of such representations is that they are stable over time such that women with distorted or disengaged prenatal representations still have them at one year postpartum (Theran et al., 2005), and they predict observed parenting behaviours and child attachment at age one (Levendosky et al., 2011).

The mechanisms involved
Although we do not currently fully understood the mechanisms that may underlie foetal programming by prenatal stress in humans, a number of potential pathways have been identified. One early suggestion was a decrease in blood flow to the foetus (Teixeira et al., 1999) (i.e. elevated/chronic sympathetic nervous system stimulation caused increased release of catecholamines and vasoconstriction, altering uteroplacental blood flow reducing oxygen and calorie intake influencing foetal CNS development). However, it is not clear if the decrease observed in this study would be clinically significant, and others have failed to replicate the original finding (Mendelson et al., 2011).

A second mechanism identified in animal models involves the foetus being overexposed to glucocorticoids as a result of maternal cortisol crossing the placenta, and high CRH levels in the foetus influencing the brain development and HPA-axis regulation, and autonomic and endocrine functioning of the foetus, and later the infant and child. However, the human HPA axis functions differently in pregnancy from most animal models, because of the placental production of CRH, which in turn causes an increase in maternal cortisol. The maternal HPA axis becomes gradually less responsive to stress as pregnancy progresses (Kammerer et al., 2002), and there is only a weak, if any, association between maternal mood and her cortisol level, especially later in pregnancy (O’Donnell et al., 2009). It thus seems unlikely that an increase in maternal cortisol is the mediating mechanism between prenatal maternal stress, anxiety or depression in later pregnancy and altered foetal outcome.

However, another mechanism by which the foetus could become overexposed to glucocorticoids that has been demonstrated in both rats (Mairesse et al., 2007) and humans (O’Donnell et al., 2012) in the absence of increases in maternal cortisol levels, is the impact of stress on transplacental transfer, through changes in placental function, especially the enzyme 11b-hydroxysteroid dehydrogenase type II the barrier enzyme which converts cortisol to the inactive cortisone.

Serotonin is another possible mediator of prenatal stress induced programming effects on offspring neurocognitive and behavioural development. During gestation serotonin regulates cell division, differentiation and synaptogenesis (Oberlander et al., 2009). Animal studies have shown that increased serotonin exposure during gestation is associated with alterations in many neuronal processes and subsequent changes in offspring behaviour. Recent work has identified an endogenous serotonin biosynthetic pathway in the human placenta (Bonnin et al., 2011), suggesting a possible role for alterations in placental serotonin in human foetal

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programming.

Epigenetic changes, which can be induced by the environment and involve reversible changes to the structure of DNA (i.e. such as the addition of a methyl group, control the amount of mRNA and protein produced, may underlie many of the processes of foetal programming. Prenatal stress has been shown to cause epigenetic changes to the rodent brain, in the DNA that codes for the receptor that binds the stress hormone cortisol (Mueller and Bale, 2008). In humans, stress during pregnancy caused by violence from the partner, has been shown to cause epigenetic changes in the DNA for this same receptor, in the blood of their adolescent children (Radtke et al., 2011).

Clinical magnitude of the effects of prenatal stress

The magnitude of many of the effects described above are not just statistically significant but also clinically significant. In the large ALSPAC population study it was found that if the mother was in the top 15 per cent for anxiety, her child was at double the risk for emotional/behavioural problems at ages four and seven (O’Connor et al., 2002, 2003) after controlling for a wide range of possible confounders including postnatal maternal mood. The risk was raised from about 5 per cent in the general population to about 10 per cent in the children of the high anxiety group. Most children were not affected, and those that were, were affected in different ways. It is possible to calculate from this that the attributable risk of childhood behavioural problems due to prenatal stress is about 10-15 per cent (Talge et al., 2007). Similar results have been obtained for older children (i.e. 13 years old – unpublished observations).

The effects of prenatal stress on cognitive development also appear to be clinically significant. In a study correlating prenatal life events with child cognitive development at 17 months, Bergman et al. (2007) found that prenatal stress accounted for 17 per cent of the variance in cognitive ability, after controlling for a range of confounders, including postnatal maternal mood. Prenatal partner relationship strain accounted for most (73 per cent) of the life event stress related variance in cognitive ability. If the woman said she had suffered from three or more prenatal partner related life events (e.g. “your partner was emotionally cruel to you”) her infant had a mean Bayley Mental Developmental index of 89, compared with 98 for the rest of the group (the general population norm being 100). King and Laplante (2005) found even greater effects on cognitive ability, when they examined two-year-old children of mothers who had been exposed to a Canadian ice storm during pregnancy, and compared the outcome for those who had been exposed to high or low stress. For children of mothers exposed to high stress in the first or second trimesters the Bayleys’ scores were 14 and 19 points, respectively, lower than the children of the low stress mothers.

What works to improve maternal psychological wellbeing in pregnancy

This research provides an indication not only of the importance of intervening during pregnancy to reduce the risk of adverse maternal mental health impacting child development as a result of foetal programming, but also suggests what the focus of such interventions should be.

The Healthy Child Programme (Department of Health (DH), 2009) provides the policy context for the delivery of a range of Universal (i.e. delivered to all pregnancy women), Universal Plus (i.e. delivered to women with moderate level need) and Universal Partnership Plus (i.e. delivered to women with high level need) level interventions, which are described below in more detail.

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Universal provision during pregnancy provides key opportunities to support wellbeing and to identify women who may be in need of additional support. The NICE Guidelines on mental health in pregnancy and the postnatal period (NICE, 2007) recommend that midwives are trained to detect depression and offer support, and that they undertake screening to identify common mental health problems at booking-in and subsequent visits using simple tools such as the Whooley questions. Midwife led care in the community during the antenatal and postnatal period using evidence-based guidelines can also be effective in improving maternal mental health (MacArthur et al., 2003).

Similarly, the Healthy Child Programme recommends the delivery of an Antenatal Promotional Interview by the health visitor at 28 weeks (DH, 2009). The Promotional Interview is conducted using the Antenatal Promotional Guide, which consists of a flexible and semi-structured framework of questions that is conducted with both parents. The interview provides the health visitor with the opportunity to both support wellbeing and to identify women who may be experiencing high levels of stress, anxiety or depression, or who are not showing a good level of bonding with the foetus, in order to provide additional support.

Although antenatal education classes have long been used as a universal method of supporting wellbeing and improving birth outcomes, a recent review found no evidence that participation in standard antenatal education programmes prevented the onset of anxiety or depression or was effective in its treatment (Schrader McMillan et al., 2009). There was some evidence to suggest that that group-based social support including antenatal preparation for parenthood classes can be effective in supporting women with sub-threshold symptoms of depression and anxiety, particularly where it involves adjuncts such as massage and music therapy (Schrader McMillan et al., 2009). This review also found some evidence to suggest that some of the new transition to parenthood programmes, which are replacing the delivery of antenatal classes in many places and that have a more explicit focus on the emotional transition to parenthood, are promising models of working in terms of promoting maternal psychological wellbeing, parental confidence, and satisfaction with the couple and parent-infant relationship in the postnatal period (Schrader McMillan et al., 2009).

Listening to music, has been found to decrease maternal plasma cortisol and self-reported state anxiety score, in pregnant women awaiting amniocentesis (Ventura et al., 2012). Maternal relaxation has also been shown to improve indices of foetal neurobehaviour, such as heart rate variability (DiPietro et al., 2008). One study that compared active (directed by a therapist) and passive (sitting in a chair) relaxation found that while both active and passive relaxation significantly reduced State Anxiety and maternal heart rate, the effect was significantly greater with the active relaxation (Teixeira et al., 2005). In contrast, the passive relaxation significantly reduced noradrenaline levels whereas active did not. Both methods significantly reduced cortisol. This study showed that there can be a lack of correlation between psychological and biological measures. This implies that interventions that reduce maternal psychological symptoms will not necessarily change the relevant biological factors for foetal programming, and each intervention will need to be tested for its effect on child outcome.

Other effective psychosocial and psychological interventions for preventing postnatal depression for pregnant and new (up to six weeks postpartum) mothers, including both women with no known risk and

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those with risk of postpartum depression, include professional and lay support – home visiting, peer support
and interpersonal psychotherapy (Dennis and Dowswell, 2013).

A number of new approaches to working now focus on the provision of group-based support to high risk
groups of women during pregnancy aimed at building maternal reflective function to promote bonding and
help the mother to reflect on what this baby might be like, with the long-term aim of improving infant
attachment security (Jenkins and Williams, 2008).

Universal Plus
Universal Plus interventions are targeted at women who have been identified as having mild to moderate
problems and who need additional support. The NICE guidelines (NICE, 2007) recommend that women who
require psychological treatment should receive an appointment within one month of the initial assessment
(and no more than three months). Treatments that are recommended for mild to moderate problems
include self-help strategies (e.g. guided self-help; computerised cognitive-behavioural therapy (CBT) or
exercise); non-directive counseling delivered at home (e.g. listening visits); brief CBT or interpersonal
psychotherapy.

A recent systematic review of mind-body interventions during pregnancy for preventing or treating women's
anxiety identified eight RCTs evaluating hypnotherapy (one trial), imagery (five trials), autogenic training (one
trial) and yoga (one trial), and found some evidence of effectiveness for the use of imagery and autogenic
training on anxiety during delivery and the immediate postpartum period only (Marc et al., 2011).

There is also emerging evidence to suggest that mindfulness-based stress reduction and a modified form
based on CBT called mindfulness-based cognitive therapy can be effective in improving mood states when
delivered during pregnancy (Vieten and Astin, 2008). The Nurse Family Partnership intensive home visiting
programme is effective in improving health behaviours in pregnancy of teenage mothers, including reducing
alcohol use (Olds et al., 1986).

Universal Partnership Plus
Women experiencing severe anxiety or depression during pregnancy should be referred to their GP who will
discuss with them the potential risks and benefits associated with the use of ante-depressants (NICE,
2007). Psychosocial and psychological interventions that have been shown to reduce anxiety and stress
include applied relaxation training (Bastani et al., 2005), and massage therapy, which can improve depression
and other outcomes (e.g. prematurity and low birthweight; Field et al., 2004). Interpersonal psychotherapy
has also been shown to be effective for pregnant women meeting DSM-IV criteria for major depression
(Spinelli and Endicott, 2003).

A range of interventions have been shown to reduce PTSD associated with interpartner violence including
individual trauma-focused cognitive-behavioural therapy (TFCBT), eye movement desensitisation and
reprocessing, stress management and group TFCBT (Pissoon, 2009). Counselling (NICE, 2013) and forgiveness
therapy (NICE, 2013) have also been shown to reduce symptoms of depression and PTSD.

Brief behavioural counseling (Whitlock et al., 2004) and contingency management (Terplan and Lui, 2007) are
two of the few evidence-based interventions that have been shown to help improve the dependency of

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alcohol/substance dependence women but with no evidence about their benefits in terms of anxiety and depression.

Clear care pathways should be established for women experiencing substance dependency, interpartner violence or severe mental health problems, and should involve referral to social services for a prebirth assessment and additional support including the input of specialist practitioners.

Summary

There is extensive evidence showing that the psychological wellbeing of women in pregnancy can have long-term effects on the child, especially in terms of their later emotional and behavioural adjustment. This evidence points to the importance of intervening during pregnancy to provide support that is aimed at reducing stress, anxiety and depression, and promoting reflective function. Although a number of evidence-based methods of working to promote the mental wellbeing of women during pregnancy are currently available, innovative ways of working are still being developed, and further research is needed to identify effective treatments for women experiencing severe problems such as substance dependency and interpartner violence. Much more still needs to be done to ensure that the treatment of common mental health problems in pregnancy is routinely addressed. This will help the women themselves and in the long-term should help their children also.

Summary of implications for policy and practice:

- The psychological wellbeing of women in pregnancy can have long-term effects on the child, especially in terms of their later emotional and behavioural adjustment.
- This evidence points to the importance of intervening during pregnancy to provide support that is aimed at reducing stress, anxiety and depression, and promoting reflective function.
- A number of evidence-based methods of working to promote the mental wellbeing of women during pregnancy are currently available, and should be implemented.
- More still needs to be done to ensure that the treatment of common mental health problems in pregnancy is routinely addressed.

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