How the emotional state of the mother during pregnancy can affect the development of the fetus and the child—the importance of the relationship with the partner

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Imperial College London

One plus One  Feb 2008
From fetus

To child
• Women have more symptoms of depression and anxiety during pregnancy than postnatally

• Pregnancy can also be a time of increased domestic abuse and relationship strain
Domestic abuse during pregnancy
Low income Hispanic population

- The prevalence of abuse during pregnancy:
  - verbal abuse 46.9%
  - physical abuse 7.6%
  - sexual abuse 5.8%

Fetal programming

Environment in utero, during critical periods, can alter the development of the fetus, with a permanent effect on the phenotype.
The fetal origins of adult disease hypothesis

David Barker

Coronary heart disease, Type 2 diabetes, stroke and hypertension originate in developmental plasticity, in response to undernutrition during fetal life
The programming hypothesis brings a new perspective to public health. Diseases that were once thought to arise near the time of their manifestation in adult life are now known to have roots in pre- and early post-natal life....
Evil eye

Many societies have believed that maternal emotions during pregnancy could affect the development of the baby in the womb.
Educational Poster for Expectant Mothers

National Child Welfare Association 1919
Effects of prenatal stress

-animal studies
Effect of Stress During Pregnancy on the Adult Offspring Rat.

All offspring were fostered on the 1st day after birth to non-stressed dams.
Wide range of effects

- More anxiety
- Reduced attention
- Learning deficits
- Reduced laterality
- Altered sexual behaviour
Long term effects of prenatal stress on offspring of non human primate

More anxiety
Lower attention span

HPA axis hyperactivity
(greater cortisol responses)

Mimicked by giving ACTH to the mother-blocked by adrenalectomy

Schneider et al
Dopamine Receptor Imaging

**Dopamine D$_2$ receptor imaging**

[$^{18}$F]fallypride in the rhesus monkey
(horizontal section, OM+17mm)
DVR Ratio for FAL to FMT

Ratio: \( \frac{\text{DVR FAL}}{\text{DVR FMT}} \)
Effects of prenatal stress in humans?
Links between maternal anxiety and fetal behaviour and heart rate

e.g. Study shown that if pregnant mothers are asked to do a mental arithmetic test

fetal heart rate goes up in the anxious group

Monk et al 2000
Antenatal stress and pregnancy outcome

- Increased risk of slower growth and smaller babies for gestational age
- Increased risk of preterm and earlier delivery
Effects of stress during pregnancy-preterm delivery

Stress accounts for about 20% of the risk for preterm delivery

May be stronger effect at >32 weeks

Preterm delivery is itself a strong risk factor for later behavioural, cognitive and emotional problems in the child.
Antenatal stress and direct effects on the child
• An early observational study was by DH Stott in 1965 a GP in Scotland.

• Information was collected from 200 women in 1965-6, at the end of their pregnancy.

• Mother asked about her physical and mental health, the course of the pregnancy, and her social circumstances.

• The health, development, and behaviour of the child were followed for the next 4 years.
Major conclusions:

“Stresses during pregnancy involving severe and continuing personal tensions, in particular marital discord, were closely associated with child morbidity in the form of ill health, neurological dysfunction, developmental delays and behaviour disturbance.”

“The association between personal tensions during pregnancy and hyperactivity in the child appears to be a very close one”

Stott 1973
Studies showing links between antenatal stress/anxiety and child behavioural/emotional problems

- Brouwers et al 2001
- O’Connor et al 2002, 2003
- Huizink et al 2003
- Van den Bergh et al 2004, 2005
- Obel et al 2004
- Rodriguez et al 2005
ALSPAC Study. Does antenatal stress affect child behaviour in humans?

- Aim of our study:
- To determine the long term effects of antenatal stress or anxiety on the behavioural development of the child

O’Connor et al 2002, 2003
ALSPAC study

Maternal anxiety-at 18 and 32 weeks of pregnancy
Compared 15% most anxious mothers
with the rest

Child behaviour
–maternal report at 4 and 7 years old.
Strengths and Difficulties questionnaire.
Attention deficit/hyperactivity;
anxiety and depression;
conduct disorder

O’Connor et al 2002, 2003
Multivariate Analysis

Cohort with complete data
n = 7, 363

- Maternal age
- Birthweight
- Gestational age
- Smoking
- Alcohol
- Psychosocial factors: crowding, maternal education
- Postnatal depression and anxiety
Multivariate analysis - boys - 7 years
Behavioural/emotional problems and maternal antenatal anxiety at 32 weeks

O'Connor et al 2003
Multivariate analysis - girls – 7 years
Behavioural/emotional problems and maternal antenatal anxiety at 32 weeks
Links are similar with antenatal anxiety at 18 weeks gestation but less marked than at 32 weeks.

It is not just first trimester.
Relative increase in brain size

<table>
<thead>
<tr>
<th></th>
<th>Fold Increase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fetus (20-40 weeks)</td>
<td>17</td>
</tr>
<tr>
<td>Child (birth-5 years)</td>
<td>4</td>
</tr>
</tbody>
</table>

- 20 week fetus
- Birth
- 5 years
Is it antenatal anxiety or depression?

Effects less strong with depression (EPDS)
Clinical implications

• For top 15% of most anxious women in pregnancy, emotional/behavioural problem symptom rate in children doubled from 5 to 10%.

• Attributable load of behavioural/emotional problems in whole population due to antenatal stress ~ 15%
Studies showing links between antenatal stress/anxiety and impaired child cognitive outcome

- Brouwers et al 2001
- Buitelaar et al 2003
- Laplante et al 2004
- Bergman et al 2007
Questions

• Are effects really prenatal?
• Are same children affected with impaired emotional and cognitive outcomes?
• What type of prenatal stress or anxiety is most detrimental?
• What are the mediating mechanisms?
Current Study

(Bergman, Sarkar, Adams, Fisk, Modi, O’Connor and Glover)

- Women recruited at time of amniocentesis
- Maternal plasma and amniotic fluid taken for later hormone analyses
- Mother and child recalled at 17 months if child had no medical problems
- Mother recorded Life events for both antenatal and postnatal period.
- Bayleys cognitive MDI test (observer rated) and fear reactivity tests carried out when child is 17 months
Bayley Scales of Infant Development (BSID-II)

Study child’s mental (MDI) development at 17 months

Bergman et al JACAAP 2007
Association between number of antenatal stressful life events and Bayley Scales MDI score at follow-up ($r_s(125)=-0.39$, $p<0.001$)
Association between number postnatal stressful life events and Bayley Scales MDI score at follow-up ($r_s(125)=-0.05$, ns)
Antenatal life events and Bayley’s Mental Development score at 18 months

![Bar chart showing the relationship between the number of life events and MDI score. The chart indicates a significant difference (P<0.001) between the two groups, with a higher MDI score for those with fewer life events (<3) compared to those with 3 or more life events (3+).]
## Significant correlation coefficients between antenatal life event scores and child’s MDI

<table>
<thead>
<tr>
<th>Event</th>
<th>Correlation Coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>You were separated/divorced</td>
<td>-0.33**</td>
</tr>
<tr>
<td>You had a serious argument with your partner</td>
<td>-0.28*</td>
</tr>
<tr>
<td>Your partner was emotionally cruel to you</td>
<td>-0.37**</td>
</tr>
<tr>
<td>You suffered from mental illness</td>
<td>-0.24*</td>
</tr>
<tr>
<td>A friend or relative suffered from mental illness</td>
<td>-0.24*</td>
</tr>
</tbody>
</table>
Mental Developmental Index in child of those with and without relationship problems in pregnancy

Bayley Scales MDI score

P=0.01
Prenatal Stressful Life Events and Child Fearfulness

Association between number antenatal stressful life events and Lab-Tab fear reactivity score at follow-up ($r_s=0.39$, $p<0.001$)
Association between number postnatal stressful life events and Lab-Tab fear reactivity composite score at follow-up ($r_s = -0.06$, ns)
Fear reactivity in child of those with and without relationship problems in pregnancy

P=0.01
Link between Mental Development scores and Fear Reactivity scores

$r=-0.09$ (ns)
• This study has shown that stress due to relationship problems with the partner during pregnancy, can affect the women in a way that impairs the neurodevelopment of her fetus and child
It’s how you feel that matters

• Different people will respond differently to the same external psychological stress

• Social support is very important both at work and at home
How?

Mechanisms

Fetal programming and epigenetic effects
Maternal stress/anxiety/mental illness

11 b-HSD 2

? transplacental passage cortisol?

cortisol↑
Life Events questionnaire (26 items)
Spielberger state and trait Anxiety questionnaire
Correlation between maternal plasma and amniotic fluid cortisol levels (nmol/L) n = 290

$r = 0.43$ $p = 0.000$
Correlation between maternal plasma and amniotic fluid cortisol with increasing maternal anxiety

Spielberger State anxiety scores

Submitted for publication
11β-HSD2 is involved in the conversion of cortisol into a more active form in the placenta during both unstressed and stressed conditions. The diagram shows the flow from cortisol in the mother, through the placenta, and into the fetus.
Correlation between amniotic fluid cortisol and cognitive development

\[ r = -0.245 \quad n=125 \quad p=0.006 \]
Why?
Predictive adaptive value of changes due to prenatal stress in a stressful environment in the wild?

• ADHD- shifting attention helps if predators about
• Anxiety/fear reactivity- beneficial effects of more vigilance
Summary

Maternal stress/anxiety/ depression during pregnancy has a broad spectrum of adverse effects on the developing fetus and future child

- Increased behavioural and emotional problems.
- Impaired cognitive and language development.
Effects of antenatal stress are different with each child-most are not affected

Probably depends on genetic vulnerability and gene environment interaction

May be modified by sensitive postnatal care or made worse by insensitive or harsh parenting
Implications

• We need to recognize all women during early pregnancy for emotional and relationship problems, stress and anxiety.
• Then we need to provide appropriate help for each woman.
David Olds, PhD

Professor of Pediatrics, Psychiatry, and Preventive Medicine

University of Colorado Health Sciences Center
FAMILIES SERVED

• Low income pregnant women
  – Usually teens
  – Usually unmarried

• First-time parents
NURSE FAMILY PARTNERSHIP

• Program with power
  – Nurses visit families from pregnancy through child age two
  – Makes sense to parents
  – Solid empirical & theoretical underpinnings
  – Focuses on parental behavior and context

• Rigorously tested
NURSE FAMILY PARTNERSHIP’S THREE GOALS

1. Improve pregnancy outcomes
2. Improve child health and development
3. Improve parents’ economic self-sufficiency
ELMIRA SUSTAINABLE RESULTS: Benefits to Children

Abuse & Neglect \[\downarrow\] 48%

Arrests \[\downarrow\] 59%

Adjudications as PINS* \[\downarrow\] 90%
(Person In Need of Supervision) for incorrigible behavior

* Based upon family-court records of 116 children who remained in study-community for 13-year period following end of program.
Unborn babies targeted in crackdown on criminality

Blair launches policy imported from US to intervene during pregnancy to head off antisocial behaviour

Lucy Ward
Social affairs correspondent

Unborn babies judged to be at most risk of social exclusion and turning to criminality are to be targeted in a controversial new scheme to be promoted by Downing Street today.

In an attempt to intervene as early as possible in troubled families, first-time mothers identified just 16 weeks after conception will be given intensive weekly support from midwives and health visitors until the unborn child reaches two years old.

Unveiling the findings of a Downing Street review, Tony Blair will make clear the government is prepared to single out babies still in the womb to break cycles of deprivation and behaviour.

He will also acknowledge that the state must do more to help minority of families and will stress that the support they need cannot come through the promotion of marriage.

In an attempt to draw a clear division between Labour and the Conservatives Mr Blair will say that making marriage the primary focus of family policy will be ineffective and could lead to discrimination.

The support includes help with giving up smoking or drug use in pregnancy, followed by a focus on bonding with the new baby, understanding behaviour such as crying, and encouraging a mother to develop her skills and resources to be a good parent. The programme is voluntary and the intention is to capitalise on the so-called "magic moment" when parents are receptive to support for themselves and their baby.

In the US, three large trials have seen consistently positive results, including higher IQ levels and language development in children, lower levels of abuse, neglect and child injuries in families, and improvements in the antenatal health and job prospects of mothers.

Proponents of the scheme, pioneered by the American paediatrician Professor David Oks, also point to the long-term cost savings, estimated at almost £25,000 ($32,500) by the time a child is 30.

The decision to target unborn babies is, in effect, an acknowledgement by Mr Blair that the government's focus on tackling social exclusion has left a hard-core - 2% - of the most excluded families behind.

The prime minister's introduction to today's family review says the state must help such children out of unfairness, and

Madeleine: police lack evidence to hold suspect

Giles Tremlett Prada da Luz

A British expatriate yesterday became the first formal suspect in the disappearance of four-year-old Madeleine McCann, with police admitting he was the main focus of their investigation.

But detectives said they did not have enough evidence to charge Robert Murat under Portuguese law. The 33-year-old estate agent was released after questioning but he will not be allowed to leave the country and will have to report to police on a regular basis.

Family and friends of Mr Murat immediately protested his innocence and his mother, Jenny, whose home is 150 metres from where Madeleine went missing, said her son was worried police had picked on him because they were desperate to find a British suspect.

Mr Murat last night told Sky News he was being made a scapegoat and the investigation "had ruined his life".

In unusual move, the Association of Chief Police Officers and the Crown Prosecution Service also expressed concern about some reporting of the case.

At a press conference yesterday, the lead investigating officer, Chief Inspector Olegario Sousa, gave few details about the inquiry but confirmed that the main line of investigation related to five properties searched on Monday, the most significant being Casa Lilianna, the house Mr Murat shares with his mother.

Mr Sousa seemed more hopeful that his team had promising leads, but admitted he will look twice at rumour and circumstantial ties...
The aims of the family nurse partnership—
how reduction in antenatal stress may help

- Better physical *health-less preterm delivery and larger babies*

Educational *success-better cognitive development*

- Better mental *health-less anxiety and behavioural problems*

- Less *crime-less conduct disorder, ADHD and improved cognitive development*
Public health implications of reducing stress/anxiety/depression in pregnancy

• More than one million children in UK suffer from neurodevelopmental disorders
• Attributable load of neurodevelopmental problems due to prenatal stress 10-15%
• Potential to reduce number of affected children in the UK by 100,000-150,000