Antenatal depression and offspring psychopathology: the influence of childhood maltreatment

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Background
Antenatal depression and childhood maltreatment have each been associated with offspring psychopathology, but have never been examined in the same sample.

Aims
To determine whether childhood maltreatment influences the association between antenatal depression and offspring psychopathology.

Method
Prospectively collected data on antenatal depression, offspring maltreatment (age 11) and offspring psychopathology (age 11 and 16) were analysed in 120 mother–offspring dyads from the community-based South London Child Development Study.

Results
Antenatal depression increased the risk of maltreatment in the offspring by almost four times. Children exposed only to antenatal depression or only to childhood maltreatment were no more at risk of developing psychopathology; however, children exposed to both antenatal depression and childhood maltreatment were at almost 12 times greater risk of developing psychopathology than offspring not so exposed.

Conclusions
Research investigating exposure to adverse events in utero and offspring psychopathology should take account of postnatal adverse events such as maltreatment.

Declaration of interest
None.

Correlation is not causation. A recent editorial in this Journal warns against assuming that associations between exposure to adverse events in utero and later offspring psychiatric disorder imply causation, because postnatal events may confound the association between exposure to prenatal events and later childhood or adulthood difficulties. There have been many studies suggesting that exposure to antenatal maternal psychopathology has particular effects that are distinct from exposure to postnatal events. For example, we have shown in a prospective study of women who were pregnant in 1986 and their offspring that exposure to antenatal depression in utero is associated with adolescent offspring having depression and antisocial problems. Another study on a much larger cohort has found an association between exposure to antenatal anxiety in utero and children's emotional and behavioural problems at age 4. None of the associations described above is present when offspring are exposed only to postnatal (maternal) psychopathology. However, there remains the possibility of what Thapar & Rutter call ‘unrecognised, unmeasured “residual” confounding not tapped by the available measures’. Oates also cautions us against the risk that such research may lead to ‘distraught mothers blaming themselves’ when something does not go well for the offspring. Hence the importance of testing the effects of newly identified potential confounders in the associations between antenatal events and offspring outcome, in order to guarantee the quality of information given to pregnant mothers.

One such important confounder, which has not yet been examined in this context, is childhood maltreatment. There is substantial research evidence showing that childhood maltreatment is associated with a high risk of developing adult depression and adult antisocial behaviour. For example, retrospective reporting of childhood maltreatment (psychological abuse, sexual abuse, physical abuse, neglect) has been shown to be associated with a significant increase in lifetime depression for both men and women. So, could childhood maltreatment be a yet unrecognised ‘residual confounder’ in the association between exposure to maternal depression in utero and psychopathology in offspring? There is some evidence suggestive of an association between perinatal events and later childhood trauma. Zhou et al. identified the offspring of young, unmarried mothers who smoked in pregnancy and had inadequate prenatal care, as particularly vulnerable to maltreatment. However, they did not examine antenatal depression, and, to our knowledge, nobody has investigated the association between antenatal maternal depression and occurrence of childhood maltreatment in the offspring. If antenatal depression is associated with childhood trauma, it may not be exposure to maternal depression in utero that explains later childhood psychopathology, but rather, the experience of childhood trauma. We thus test three specific hypotheses:

(1) there is an association between maternal antenatal depression and experience of childhood maltreatment in the offspring;

(2) maltreatment in childhood influences the effect of maternal depression in pregnancy on adolescent offspring psychopathology;

(3) hypothesis 2 remains true independently of the mother’s own history of childhood abuse, her own perceived emotional security within her family of origin, her current family stress and the chronic nature of her depression.

Method
Participants
In total, 120 women were included in this study. They represent 77% of a random sample of 155 pregnant women who were recruited into the South London Child Development Study in 1986 and provided information on their mental health when they were 36 weeks pregnant. In subsequent follow-up assessments, these 120 women and the index children independently provided information on the children’s experiences of maltreatment at age...
11 and psychopathology at ages 11 and 16. Methods have previously been described.2,3,11 Demographic characteristics of this sample are presented in Table 1.

### Measures

Additional details on the measures used are described in the online supplement to this paper.

#### Maternal depression

Maternal depression was assessed at 36 weeks of pregnancy, and at 3 and 12 months postpartum. ICD-9 diagnoses were made of the women’s current mental state over the 2 weeks prior to the interview using the Clinical Interview Schedule (CIS).12

Maternal depression at 4, 11 and 16 years

Diagnoses of maternal depression, both current and retrospective to the last assessment, were made according to Research Diagnostic Criteria (RDC), using the lifetime version of the Schedule for Affective Disorders and Schizophrenia (SADS-L).13

Maternal history of childhood physical and/or sexual abuse

This was obtained 4 years after the birth of offspring.

Maternal perceived emotional security within her family of origin

A rating of emotional security was made on a 4-point Likert scale by the mother and further dichotomised into secure and insecure.

Family stress

This was measured by the number of parental relationship changes experienced during the offspring’s lifetime from 0 to 16 years.

Mothers’ juvenile conduct symptoms

We obtained mothers’ retrospective reports of their own conduct symptoms before the mothers’ age of 15.5

### Results

#### Association between exposure to antenatal maternal depression and childhood maltreatment

Of the 120 children (57 boys and 63 girls), 25 (21%) reported physical and/or sexual abuse and/or harsh parenting at 11 years. Girls and boys were equally likely to have experienced childhood maltreatment (n = 120, χ² (1) = 1.98, P = 0.16). Reports of maltreatment were not associated with maternal depression at the time of the interview (n = 116, χ² (1) = 0.52, P = 0.47) or with the child’s emotional well-being, as measured by the child’s own reports of emotional difficulties on the Strength and Difficulties Questionnaire17 (Mann–Whitney U-test, z = 0.08, P = 0.93).

Overall, 15 children (13%) reported physical abuse (n = 9) and/or sexual (n = 6) abuse at some time during their childhood, and 20 children (17%) reported experiencing harsh discipline in the 3 months prior to the interview at 11 years. Fifteen children had experienced one form of abuse, and ten children two forms. No child had experienced all three forms (see Appendix for a representative case study). Twelve children were maltreated by the biological mother (alone or with father/stepfather). Specifically, four of the nine children who experienced physical abuse had been abused by their mother (alone or with father), and five by their biological father. Of the six children who had experienced sexual abuse, none of the perpetrators was the biological mother (or father): in five cases the perpetrator was another child (in one case a sibling) and in one case a teacher.
Twelve of the 20 children who had experienced harsh discipline had been disciplined either by their biological mother \((n=8)\) or by both their biological mother and their biological father/stepfather \((n=4)\), while the remaining 8 had been disciplined by their biological father, stepfather or stepmother.

Of the 120 children, 25 (21%) were exposed to antenatal maternal depression as defined by their mothers reaching ICD-9 threshold for a diagnosis of depression at 36 weeks of pregnancy. Compared with children who had not been exposed to antenatal maternal depression, children who were exposed were significantly more likely to have experienced childhood physical or sexual abuse or harsh parenting \((n=120, \chi^2 (1) = 7.03, P = 0.008; \text{OR} = 3.6, 95\% \text{ CI} 1.4–9.4)\) by the age of 11 years (Table 2), thus confirming hypothesis 1. In contrast, neither maternal depression after the birth nor maternal depression at any other time during the child’s first 11 years was associated with the children’s experience of abuse \((n=116–119, \text{all } \chi^2 (1) < 1.04, P \text{ values } > 0.30)\). As mentioned above, of the 25 children who had been maltreated, 12 were maltreated by the biological mother (alone or with father/stepfather); however, there was no association between antenatal depression and whether or not the perpetrator of the maltreatment was the biological mother \((n=25, \chi^2 (1) = 0.03, P = 0.87)\). In other words, having antenatal depression did not increase the risk of the mothers themselves being the perpetrators of the maltreatment. Furthermore, there were no significant effects of maternal juvenile conduct symptoms (Mann–Whitney U-test, \(z=1.14, P=0.25\)) or of the biological fathers’ history of arrests \((n=113, \chi^2 (1) = 0.49, P=0.48)\) on risk of offspring maltreatment.

### Offspring psychopathology

Thirty-six children (30%) were given a diagnosis of either a depressive disorder \((n=21)\) or conduct disorder \((n=22)\) at 11 and/or 16 years. Seven had comorbid diagnoses. There was a significant association between the two sets of disorders \((n=119, \chi^2 (1) = 4.3, P=0.04)\). There were no significant gender differences.

### Exposure to antenatal maternal depression and/or childhood maltreatment, and offspring psychopathology

Logistic regression analysis was used to test the hypothesis that any association between antenatal maternal depression and adolescent offspring psychopathology might be explained by maltreatment in childhood. Of the 25 offspring whose mothers had depression in pregnancy, 52% \((n=13)\) were diagnosed with either a depressive disorder or conduct disorder, as opposed to 24% of offspring \((n=23)\) whose mothers had not had depression \((\chi^2 (1) = 7.3, P=0.007; \text{OR} = 3.4, 95\% \text{ CI} 1.3–8.5)\). This is an extension of our previously published findings.\(^2,17\) Of the 25 offspring who had been maltreated, 48% \((n=12)\) were diagnosed with a psychiatric disorder, in contrast to 25% \((n=24)\) who had not been maltreated \((\chi^2 (1) = 4.9, P=0.027; \text{OR} = 2.7, 95\% \text{ CI} 1.1–6.8)\). Therefore, in univariate analysis, both antenatal depression and childhood maltreatment separately predict offspring psychopathology.

The first logistic regression model tested for associations with antenatal maternal depression and childhood maltreatment, and for the two-way interaction between them. When antenatal depression was entered at the first step, it significantly predicted offspring psychopathology (Wald statistic = 6.85, d.f. = 1, \(P=0.009; \text{OR} = 3.4, 95\% \text{ CI} 1.4–8.5\)). When childhood maltreatment was entered at the second step, it did not significantly predict offspring psychopathology, and antenatal depression continued to predict offspring psychopathology (Wald statistic = 4.81, d.f. = 1, \(P=0.03; \text{OR} = 2.9, 95\% \text{ CI} 1.1–7.4\)). Therefore, childhood maltreatment did not mediate the effect of antenatal depression on offspring psychopathology. Finally, when the interaction was entered at the third step, the model was significant \((\chi^2 (3) = 12.40, P=0.006)\): neither antenatal depression nor childhood maltreatment independently predicted offspring psychopathology, but the presence of both did. Specifically, in a second logistic regression analysis, the interaction of antenatal depression and childhood maltreatment, entered at the first step, significantly predicted offspring psychopathology (Table 3(a)). The children who had been exposed to both maternal antenatal depression and to childhood maltreatment were almost 12 times as likely to have psychopathology, either in the form of a depressive disorder or in the form of conduct disorder. In contrast, children who were exposed only to maternal antenatal depression or childhood maltreatment were no more at risk of having any psychopathology. This finding remained unchanged when controlling for the mother’s own experience of childhood abuse and lack of emotional security, for the child’s exposure to chronic maternal depression and to parental relationship changes (see analyses in the online supplement).

### Table 2: Exposure to maternal depression in utero and experience of childhood maltreatment

<table>
<thead>
<tr>
<th>Childhood maltreatment</th>
<th>Exposure to depression in utero</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>No, % (n)</td>
<td>Yes, % (n)</td>
<td>---</td>
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<td>---</td>
</tr>
<tr>
<td>84.2 (80)</td>
<td>15.8 (15)</td>
<td>---</td>
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</tr>
<tr>
<td>60.0 (15)</td>
<td>40.0 (10)</td>
<td>---</td>
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<td>---</td>
</tr>
</tbody>
</table>

\(\chi^2 (1) = 7.03, P=0.008\).

### Table 3: Logistic regression models with the indicators of exposure to maternal depression in utero and to maltreatment in childhood in the prediction of child and adolescent psychopathology \((n=119–120)\)

<table>
<thead>
<tr>
<th>Predictor variables</th>
<th>(\beta) (S.E.)</th>
<th>Lower</th>
<th>EXP(B)</th>
<th>Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) Any psychopathology (depression and/or conduct disorder)(^a) Depression (\times) maltreatment</td>
<td>2.46 (0.82)</td>
<td>2.35</td>
<td>11.71</td>
<td>58.47</td>
</tr>
<tr>
<td>(b) Depressive disorder(^b) Depression (\times) maltreatment</td>
<td>1.48 (0.72)</td>
<td>1.07</td>
<td>4.38</td>
<td>17.98</td>
</tr>
<tr>
<td>(c) Conduct disorder(^c) Depression (\times) maltreatment</td>
<td>2.69 (0.74)</td>
<td>3.44</td>
<td>14.78</td>
<td>63.51</td>
</tr>
</tbody>
</table>

\(a\). Any disorder: \(R^2=0.09\) (Cox and Snell), 0.13 (Nagelkerke); Model \(\chi^2 (1) = 11.80, P<0.001\).

\(b\). Depressive disorder: \(R^2=0.03\) (Cox and Snell), 0.05 (Nagelkerke); Model \(\chi^2 (1) = 3.83, P=0.05\).

\(c\). Conduct disorder: \(R^2=0.11\) (Cox and Snell), 0.19 (Nagelkerke); Model \(\chi^2 (1) = 14.49, P<0.001\)
Exposure to antenatal maternal depression and/or childhood maltreatment, and offspring depression

These findings hold true also when depressive disorder and conduct disorder are assessed separately. Of the 24 offspring whose mothers had depression in pregnancy, 8 (33%) were diagnosed with a depressive disorder at 11 and/or 16 years as opposed to 14% of offspring (n = 13) whose mothers had not had depression (χ² (1) = 5.1, P = 0.024; OR = 3.2, 95% CI 1.1–8.8). Of the 24 offspring who had been maltreated by the age of 11 years, 6 (25%) were diagnosed with depression at 11 and/or 16 years, in contrast to 16% (n = 15) who had not been maltreated. This association was not significant (χ² (1) = 1.12, P = 0.29; OR = 1.8, 95% CI 0.61–5.2).

In the first logistic regression analysis, the significant main effect of antenatal depression became non-significant when the interaction with childhood maltreatment was entered into the analysis. In the second logistic regression analysis, the interaction of antenatal depression and childhood maltreatment, entered at the first step, significantly predicted offspring depression (Table 3(b)). Offspring who had been exposed both to maternal depression in utero and to childhood maltreatment were 4.4 times more likely than those exposed to neither, to have a diagnosis of a depressive disorder at 11 and/or 16 years. In contrast, children who were exposed only to maternal antenatal depression or to childhood maltreatment were no more at risk of having depression. The finding remained unchanged when controlling for the mother’s current depression at 11 years and 16 years, which did not add significantly (Wald statistic = 0.86, d.f. = 1, P = 0.35) to the variance accounted for by the interaction between antenatal depression and childhood maltreatment.

Exposure to antenatal maternal depression and/or childhood maltreatment, and offspring conduct disorder

Of the 25 offspring whose mothers had depression in pregnancy, 9 (36%) were diagnosed with conduct disorder at 11 and/or 16 years as opposed to 14% of offspring (n = 13) whose mothers had not had depression (χ² (1) = 6.6, P = 0.01; OR = 3.6, 95% CI 1.3–9.7). Of the 25 offspring who had been maltreated by the age of 11 years, 10 (40%) were diagnosed with conduct disorder at 11 and/or 16 years, in contrast to 13% (n = 12) who had not been maltreated (χ² (1) = 9.9, P = 0.002; OR = 4.6, 95% CI 1.7–12.6).

In the first logistic regression analysis, the significant main effects of both antenatal depression and of maltreatment on offspring conduct disorder became non-significant when the interaction with childhood maltreatment was entered into the analysis. In the second logistic regression analysis, the interaction of antenatal depression and childhood maltreatment, entered at the first step, significantly predicted offspring conduct disorder (Table 3(c)). Offspring who had been exposed both to maternal depression in utero and to childhood maltreatment were 14.5 times more likely than those exposed to neither, to have a diagnosis of conduct disorder at 11 and/or 16 years. In contrast, children who were exposed only to maternal antenatal depression or to childhood maltreatment were no more at risk of having a conduct disorder. The finding remained unchanged when controlling for the mother’s own juvenile conduct symptoms, which did not add significantly (Wald statistic = 3.08, d.f. = 1, P = 0.08) to the variance accounted for by the interaction between antenatal depression and childhood maltreatment.

Discussion

Here we demonstrate for the first time that antenatal maternal depression is associated with an increased risk of the offspring being subjected to childhood maltreatment. Moreover, we also find that the association between antenatal depression and offspring psychopathology is only due to the high prevalence of depression and of conduct disorder (OR of approximately 4.4 and 14.8 respectively) in children exposed to both antenatal depression and childhood maltreatment – not in those with either one or the other exposure. In other words, although antenatal depression is associated with both offspring exposure to childhood maltreatment and with offspring psychopathology, childhood maltreatment does not mediate the effect of antenatal depression on offspring psychopathology, but rather acts as a moderator. Our findings are strengthened by the fact that the assessment of both risk factors (depression in pregnancy, maltreatment at age 11) and outcomes (psychopathology at age 11 and/or 16) were conducted prospectively, in a unique longitudinal study that has been following up mothers and their offspring from pregnancy, more than 20 years ago.23

Exposure to antenatal depression and childhood maltreatment

The association between antenatal maternal depression and offspring childhood maltreatment is a completely novel finding. The association between lifetime psychopathology in mothers and increased risk of childhood maltreatment in offspring has been described before – but never in the context of the perinatal period. Specifically, certain maternal personality attributes have been associated with offspring maltreatment, such as low self-esteem, negative affectivity (depression and anxiety) and antisocial behaviours.19 In a recent study, Kaplan et al20 found that mothers of physically abused adolescents have more unipolar depressive disorders than comparison mothers. However, no other study, of which we are aware, has assessed maternal psychopathology in the perinatal period for mothers of maltreated children. Only Oliver,21 when describing a case series of 147 extremely complex families with multiagency involvement and a history of cross-generational childhood maltreatment, noticed that 7 (out of 147) mothers had been diagnosed with postpartum depression by their treating psychiatrist, but that all of them were reclassified at some point in later years as having a personality disorder. Our study therefore is the first methodologically sound, prospective study able to assess the impact of maternal perinatal psychopathology on the risk of the offspring being maltreated.

Our data point to a specific effect of antenatal, rather than postnatal, depression, in increasing the risk of childhood maltreatment. Indeed, the effect remains, even when we account for the fact that almost all the mothers who had depression in pregnancy went on to have further depressive episodes during their children’s lifetimes. Clearly, the mechanisms underlying this specific effect are as yet unknown, and further research on this is required. Indeed, a variety of pathways may explain this finding, including putative effects of antenatal depression on attachment, offspring temperament or a mother’s ability to protect her young from maltreatment by other family members.22 However, it is important to highlight two key aspects of our results: first, our study does not suggest that mothers who have depression in pregnancy are more likely to be perpetrators of the maltreatment; and second, these analyses refer to women who had depression in pregnancy more than 20 years ago. It is possible that this association would be no longer present today, thanks to the increased emphasis on psychosocial support and treatment for women with antenatal depression. Clearly, this must be tested in more recent cohorts; but in the meantime, one can only continue to advocate assertive treatment of depression during pregnancy23.
and governmental support for Foundation Years services beginning in pregnancy.24

Interestingly, our data are consistent with observations available from preclinical and clinical studies. Specifically, Champagne & Meaney25 have observed that stress during gestation alters maternal behaviour in the rat by reducing pup maternal care (‘licking and grooming’) in lactating mothers previously characterised as expressing high levels of maternal care. It is of note that rat maternal behaviour is very stable, and this makes the impact of stress during gestation even more relevant. Moreover, lactating mothers who have been subjected to gestational stress also show a reduction of the brain expression of the receptor for oxytocin, a neurotransmitter regulating maternal care and social behaviour, which in turn may be due to a stress-induced increase in glucocorticoid hormones during gestation.25 Consistent with these preclinical data, we have recently shown that depression during pregnancy is associated with increased levels of glucocorticoids,26 and another clinical study has shown that plasma oxytocin levels of women during pregnancy and the postpartum period are related to maternal bonding behaviours postnatally.27 Therefore, it is possible to speculate that biological abnormalities induced by depression during pregnancy, such as elevated glucocorticoids,26 may alter the oxytocin system and thus contribute to changes in maternal care. This biological pathway may be in addition to psychological and psychosocial pathways that could also affect maternal care and protection following antenatal depression.

**Childhood maltreatment and child psychopathology**

The relationship between childhood maltreatment and child psychopathology has been well documented, but all the evidence comes from studies in samples of children who have been abused.29,30 Indeed, large community studies have found less comes from studies in samples of children who have been abused.29,30 Indeed, large community studies have found less evidence that childhood sexual abuse increases the risk of being a polysubstance misuser32 and of engaging in risky sexual behaviours33 in adolescence. Therefore, it is reassuring that in our prospective studies, as in other similar community ones, not all children exposed to maltreatment express frank psychopathology. We clearly show that the previous exposure to antenatal depression is indeed one of the moderating factors determining why some children do develop psychopathology when exposed to maltreatment.

**Maternal depression, childhood maltreatment and child psychopathology**

We find that it is really the co-occurrence of maternal depression and childhood maltreatment that leads to offspring depression and conduct disorder. Indeed, only exposure to both depression in utero and to maltreatment in childhood is associated with depression and conduct disorder in childhood and adolescence. This is also a completely novel finding. The association between lifetime maternal mental illness and child mental illness in offspring victims of maltreatment has been described before, but never in the context of the perinatal period, and usually in small case–control studies rather than epidemiologically based cohorts. For example, Kaufman et al34 reported that in 26 children with a history of maltreatment and of major depression, their first-degree relatives had approximately a ninefold increased risk for major depression and a three- to ninefold increased risk for other disorders such as antisocial personality, alcohol and substance dependence. Similarly, De Bellis et al,35 in a case–control study of 53 children from maltreating families referred to a clinical service for post-traumatic stress disorder, showed that mothers of maltreated children exhibited a significant lifetime incidence of anxiety disorders (58%, especially post-traumatic stress disorder), mood disorders (72%, indicating major depression and dysthymia), and alcohol and/or substance misuse or dependence disorder (32%). The majority of the children (72%) had comorbid diagnoses involving both emotional and behavioural regulation disorders.35 Because our data point to a specific effect of antenatal depression in increasing the risk of offspring maltreatment, it is tempting to speculate that the association between lifetime maternal mental illness and childhood psychopathology in offspring victims of maltreatment described in these studies may indeed be due to maternal mental illness already active in the antenatal period. However, none of these studies has addressed this hypothesis.

**Other potential confounders**

We began our introductory argument by describing the importance of potential confounders when examining the association between two variables. Therefore, having clearly demonstrated the moderating effect of childhood maltreatment in the association between exposure to antenatal depression and offspring psychopathology, we have also examined some other potential contributory factors – namely: the mother’s own experience of childhood abuse and her perception of an emotionally insecure childhood (both of which predicted maternal depression in pregnancy); current family instability (measured by the number of relationship changes that the offspring experienced during their lifetime); and the chronic nature of mothers’ depressive illness. Even after accounting for the potential confounders, the significant effect of the double exposure to maternal depression in pregnancy and maltreatment during childhood remained.

**Limitations**

The number of study participants is small and limited to a city population with high levels of social and economic deprivation and high levels of adolescent psychopathology. It is therefore difficult to generalise the findings presented here to other socioeconomic groups and geographical locations. Furthermore, although the prevalence rates of maternal depression in this community cohort are high, the low levels of other psychiatric disorders (substance misuse, personality disorders, post-traumatic stress disorder) preclude an investigation of their association with antenatal depression and childhood maltreatment, and of their impact on offspring psychopathology. In addition, the small sample size made it difficult to separate out the effects of harsh discipline, physical and sexual abuse, and to compare the effects on the offspring of maltreatment made by different perpetrators. Moreover, reports of sexual abuse at 11 years were limited to peer and sibling involvement of the child in activities for the purpose of their own sexual gratification, and it is unclear whether children who were still living with their parents would have reported sexual abuse. For example, when the 11-year-old child in the reported case history (Appendix) was asked whether he had been sexually abused, he replied that he did not know. Only when we interview the offspring as adults will we be able to see whether the reports of sexual abuse made as children were reliable. Clearly, reassessing
the offspring as adults will be fundamental to clarifying these doubts.

Implications

Our study has implications for both clinical and biological psychiatry. From a clinical point of view, our study supports the notion that exposure to maternal antenatal depression is important in the link between childhood maltreatment and childhood psychiatric disorder: both by increasing the risk of offspring maltreatment per se, and by increasing the risk of psychopathology in the offspring when maltreatment does take place. This should inform the still controversial decision-making process around the treatment of depression in pregnancy36 and give priority to psychological, psychosocial and parenting programmes aimed at reducing antenatal depression as a pathway to reduce child and adolescent psychopathology. From a biological point of view, the mechanism by which fetal exposure to maternal depression (and, in general, to stress in pregnancy) contributes to later offspring psychopathology is still not clear. We and others have described persistent biological abnormalities in adults with a history of childhood maltreatment, which may participate in the pathogenesis of adult major depression37,38 or of adult aggressive behaviour.39 However, if childhood maltreatment is associated with antenatal depression, then it is possible that some of these biological abnormalities are due to the antenatal depression, or to the ‘double insult’ perpetrated through exposure to both maternal depression in utero and to maltreatment in childhood, rather than simply to childhood maltreatment. Indeed, stress in utero in animal models, and antenatal maternal anxiety in clinical studies, has long-lasting effects on the biology of the offspring, some resembling those described in animal models of early trauma.40 Future studies should dissect how antenatal and childhood events differentially and concomitantly contribute to biological changes that put an individual on the trajectory to adult psychopathology.

Case study: Gary

Gary is 16 years old. He has a conduct disorder. He describes how he has been in trouble with the police for breaking into a telephone box with a screwdriver and stealing the money, for vandalism and for low-level fire-setting. He has been in trouble for fighting, breaking his parents’ curfew, and running away from home. He has problems with his teachers at school. He is defiant, restless and disruptive in class. He is bullied by his peers. He is anxious about going to school. Gary does not reach criteria for a depressive disorder but suffers from low self-esteem and describes himself as ugly.

Gary was physically abused by his biological father. He describes how his father held his fingers over the gas flame until it hurt and he called out in pain, how he was hit with a belt and how he was forced to sit on the floor at night, with his hands on his head and his father’s feet holding him down, and to watch adult TV programmes.

Gary’s mother suffered from depression when she was pregnant with Gary, and was unable to protect Gary from his father’s abuse. Gary’s father left the home when Gary was 6 years old. Gary remains with his mother. The interviewer describes Gary as ‘crushed’.

References

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Online supplement

Method

Procedure

Pregnancy and the first postnatal year

Two academic general practitioners (GPs) interviewed the mothers at 36 weeks of pregnancy, and at 3 and 12 months postpartum. At each interview an assessment was made of the women's current mental state over the past 2 weeks using the Clinical Interview Schedule (CIS)\textsuperscript{12} to generate ICD-9 diagnoses. The overall agreement of the reported symptoms on the CIS from the tape-recorded interviews, given as a weighted kappa coefficient, was 0.80. Consensus ICD-9 diagnoses were made by the two GPs on the basis of the content of these interviews.

Maternal depression. We visited families at home when the children were approaching 4 years and at 11 and 16 years. At each point in time, mothers provided sociodemographic information, current and retrospective to the last visit, to one of two research psychologists who were unaware of the information collected at previous visits. Diagnoses of maternal major depression (probable and definite), minor depression (definite), and intermittent depression, both current and retrospective to the last assessment, were made according to Research Diagnostic Criteria (RDC). We used the lifetime version of the Schedule for Affective Disorders and Schizophrenia (SADS-L).\textsuperscript{13} All interviews were tape-recorded. Diagnoses were made on the basis of the content of these interviews by a senior research psychologist and a psychiatrist who had not participated in the interviews.

Antenatal maternal depression (in pregnancy) was rated as being present if an ICD diagnosis was given at the third trimester interview. A diagnosis of postpartum depression was given if the mother had a current ICD diagnosis at 3 months after the birth and a diagnosis was also made at the child's 1st birthday interview. The RDC, current and retrospective, were used in early childhood (1–4 years), middle childhood (4–11 years) and adolescence (11–16 years) to describe additional periods of maternal depression during the offspring's life. Chronic depression was calculated as the number of periods from pregnancy to 16 years during which the mother experienced a depressive episode with a range of 0–5.

Maternal history of childhood abuse. At the 4-year interview mothers were asked whether they had experienced physical and/or sexual abuse before the age of 16 years.

Maternal perceived emotional security within her family of origin. At the 4-year interview mothers were asked what their home was like as a child, before the age of 16 years. Queries were made about her parents' relationship, the home environment, financial difficulties, and how happy or miserable she felt as a child. A rating of emotional security was made on a 4-point Likert scale by the mother and further dichotomised into secure and insecure.

Family stress. This was measured by the number of parental relationship changes experienced during the offspring's lifetime from 0 to 16 years. A change was recorded when either a parental figure left the family home or a new parental figure entered the home.

Offspring depressive disorders. We report DSM-IV diagnoses of major depressive disorder, dysthymic disorder and depression not otherwise specified based on combined reports at 11 and 16 years.

Biological fathers' history of arrest. Mothers reported on the biological fathers' history of arrest at the interviews at 11 and/or 16 years. In five cases where the mother did not have custody of the child, the father was interviewed, and reported on his own history of arrest.

Children's experience of psychopathology. In tape-recorded interviews at 11 and 16 years, parents (in most cases, the biological mother) and children were independently asked, by each of two different researchers, about any psychological problems, using the Child and Adolescent Psychiatric Assessment (CAPA).\textsuperscript{14} The CAPA is a psychiatric interview for children, which elicits information about events and symptoms contributing to a wide range of DSM-IV diagnoses. A 3-month 'primary period' is used rather than a longer period, because shorter periods are associated with more accurate recall. At 11 and 16 years, DSM-IV diagnoses and symptom scales were generated by computer algorithms based on 'combined reports' where a symptom is regarded as being present if either parent or child reports it. Diagnoses were made with reference to the functional impairment or incapacities section of the CAPA and show acceptable levels of test–retest reliability.

Children's experience of maltreatment. In the same tape-recorded CAPA interviews at 11 years, parents and children were independently asked about the child's experiences of trauma in the form of severe maltreatment both within and outside of the family. Assessments apply clear and consistent definitions and thresholds for the presence of symptoms, which are determined by the interviewer through standardised but flexible questioning. A dichotomous measure of childhood maltreatment was made from the combined reports (parent and child) of the children's experiences of harsh parental discipline during the previous 3-month CAPA 'primary period', along with information about any lifetime experiences of physical or sexual abuse. Harsh parental discipline was rated if one or both parents used a harsh, restrictive or excessively physical disciplinary style, leading to punishments that were more severe than would usually be thought appropriate. Physical abuse was rated if the child had been the victim of intentional physical abuse or injury by a family member sufficiently severe to leave marks, bruises or cuts, or require medical treatment. A sexual abuse episode was rated when a person (perpetrator) had involved the child in activities for the purpose of the perpetrator’s own sexual gratification. Children were rated as having been maltreated if they had experienced one or more of these three forms of abuse. It is the first time that such data are described for this cohort.

4th, 11th and 16th birthdays

Mothers' juvenile conduct symptoms. At the visit at 16 years, we obtained mothers' retrospective reports of their own conduct symptoms before the age of 15, using the antisocial personality disorder section of the SADS-L.\textsuperscript{13} All women were asked about juvenile conduct symptoms, whether or not they screened in as possible cases of antisocial personality disorder. A 10-stem scale was constructed, summing women's reports of truancy, expulsion from school, rule-breaking, stealing, lying, running away, vandalism, underage alcohol use, underage sex and juvenile arrest (Cronbach's $\alpha = 0.75$).
Offspring conduct disorder. DSM-IV diagnoses of conduct disorder based on combined reports at 11 and 16 years are reported.

Results

Other possible confounders

We analysed four potential confounders: maternal report of her own childhood experience of physical and sexual abuse; maternal report of her own childhood as insecure; child exposure to parental relationship changes from 0 to 16 years (as a proxy for the quality of the parental relationship throughout the child’s lifetime); and chronic depression in mothers. Maternal report of her own childhood experience of physical and sexual abuse was significantly associated with more offspring psychopathology \((n = 107, \chi^2 (1) = 4.6, P = 0.03; \text{OR} = 2.6, 95\% \text{ CI 1.1–6.2})\) and was also a significant predictor of the mother’s depression in pregnancy \((n = 107, \chi^2 (1) = 12.8, P < 0.001; \text{OR} = 6.1, 95\% \text{ CI 2.1–17.8})\), but not of offspring maltreatment. However, it no longer made a significant independent contribution in the logistic regression model, where the interaction of exposure to antenatal depression and to childhood maltreatment significantly predicted offspring psychopathology \((\text{Wald statistic} = 4.59, \text{d.f.} = 1, P = 0.03; \text{OR} = 7.00, 95\% \text{ CI 1.2–41.5})\). Maternal report of her own childhood as insecure was also associated with higher levels of offspring psychopathology \((n = 107, \chi^2 (1) = 9.7, P = 0.002; \text{OR} = 4.7, 95\% \text{ CI 1.7–13.0})\) and also predicted maternal depression in pregnancy \((n = 107, \chi^2 (1) = 11.2, P = 0.001; \text{OR} = 5.6, 95\% \text{ CI 1.9–16.7})\). It was not significantly associated with offspring maltreatment. It continued to be an independent predictor of offspring psychopathology when considered within the logistic regression model \((\text{Wald statistic} = 5.48, \text{d.f.} = 1, P = 0.02; \text{OR} = 1.42, 95\% \text{ CI 1.1–1.9})\) as did the interaction between exposure to antenatal depression and childhood maltreatment in predicting childhood psychopathology \((\text{Wald statistic} = 5.05, \text{d.f.} = 1, P = 0.02; \text{OR} = 6.82, 95\% \text{ CI 1.3–36.3})\).
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