Antenatal maternal anxiety is associated with problem behaviour at age five

E.M. Loomans, O. van der Stelt, M. van Eijden, R.J.B.J. Gemke, T. Vrijkotte, B.R.H. Van den Bergh

1. Introduction

The idea that the basis for a good health and development in later life is formed in the very early stages of development has a long history [1]. Recently, programming influences of maternal distress during pregnancy on long-term behavioural and cognitive development of the offspring have received increased interest (for reviews see [2–4]).

Exposure to antenatal maternal anxiety is associated with children's problem behaviour, with different outcome patterns for both sexes. Nevertheless, effect sizes in this study were small.

1.1. Antenatal Programming

Antenatal programming of offspring behaviour has even been shown to persist well into adolescence. Antenatal maternal anxiety in early pregnancy (12 to 22 weeks) was associated with depressive symptoms in girls at the age of 15 [9] and mothers' antenatal depression significantly predicted antisocial behaviour in their offspring at age 16 [10].

So far, most of these previous studies that have investigated the association between antenatal anxiety and child behaviour are based on maternal reports [5,6] or composite scores (mother + teacher) [7,8] of child behaviour. However, considerable debate in literature exists about inconsistencies in reports on child behaviour among different informants [11]. These disparities between informants might be due (at least partially) to inherent differences in experiences that these informants share with the children; for example the home environment versus the classroom [12]. In addition, evidence is accumulating for the

1.2. Cross-informant Discrepancies

Cross-informant discrepancies have received increased interest (for reviews see [2]).

1.3. Developmental Psychology

Recently, programming by maternal stress during pregnancy is found to influence behavioural development in the offspring. Antenatal maternal state-anxiety (M = 36.7, SD = 9.8) was measured around the 16th week of gestation. Five years later, 3446 mothers and 3520 teachers evaluated 3758 children's overall problem behaviour, emotional symptoms, conduct problems, hyperactivity/inattention problems, peer relationship problems, and pro-social behaviour.

Exposure to antenatal anxiety is associated with children's problem behaviour, with different outcome patterns for both sexes. Nevertheless, effect sizes in this study were small.

1.4. Conclusion

Exposure to antenatal maternal anxiety is associated with children's problem behaviour, with different outcome patterns for both sexes. Nevertheless, effect sizes in this study were small.
influence of parental psychopathology on cross-informant discrepancies [13–16]. To sum up, although evidence concerning the association between maternal negative emotions during pregnancy with long-term behavioural outcome is accumulating, these findings were based on maternal ratings of child behaviour. Therefore, the aim of the present study was to investigate the association between antenatal maternal anxiety and problem behaviour in children at age five using both maternal as well as the child’s primary school teacher’s ratings of child behaviour.

In addition, we aimed to examine the moderating role of the child’s sex in the association between antenatal anxiety and children’s problem behaviour. Results from animal studies have indicated sex differences in the programming effects of antenatal maternal stress or anxiety [17]. In humans, antenatal anxiety or stress during pregnancy was associated with cognitive impairments [18–20]. ADHD symptoms and externalising problems [7,8] in boys and with more emotional symptoms, conduct problems [5,6] and self-reported depressive symptoms [9] in girls. Hence, both male and female offspring seem at risk for these antenatal programming effects, although in each sex these effects seem to be represented in different outcomes.

In sum, the first aim of the current study was to investigate the relation between antenatal maternal anxiety and children’s behaviour at age five. An important addition to the existing body of literature was the use of mother as well as teacher reports on child behaviour. Furthermore, because of our large community based, non-clinical sample, we were able to test the moderating effect of the child’s sex. We expected higher levels of antenatal maternal anxiety to be associated with more overall problem behaviour and more externalising problems in boys and with more internalising problems (emotional symptoms) in girls.

2. Methods

2.1. Sample

The current study is part of the Amsterdam Born Children and their Development (ABCD) study, a large community based birth cohort. Extensive information about the cohort and procedures regarding data collection is provided elsewhere [21]. In short, between January 2003 and March 2004 12,373 pregnant women were approached to participate in the study via their obstetric care provider and a questionnaire covering socio-demographic, obstetric, lifestyle and psychosocial conditions was sent to them. Currently, 6161 of the 6735 mothers (92%) who gave permission for follow-up of their child were approached for the 5th-year measurement of their child (phase III, 2008–2010). Attrition in this follow-up number is due to withdrawal, infant or maternal death and loss-to-follow-up as a result of unknown current address or emigration. The 5-years questionnaire was filled in the 5-years questionnaire.

Prior to analyses, 128 mothers were excluded from further analysis due to the presence of a severe medical condition (e.g., (pre-) pregnancy diabetes, cancer), or the use of medication (corticosteroids, antidepressants, anti-anxiety drugs, antipsychotics) during pregnancy. One hundred and eighty-seven children that were born premature (GA<33 weeks), had a low birth weight (~2500 g), or suffered from obstetric complications, cancer, congenital malformations and syndromes related to the central nervous system, were removed from the sample. Sixteen questionnaires were not filled in by the child’s birth mother; therefore these reports were not included in the analysis. After these a priori exclusions the sample consisted of 3758 children; 3446 mothers and 3520 teachers have evaluated the children’s behaviour. All participating mothers gave their written informed consent. Approval of the study was obtained from the Central Committee on Research Involving Human Subjects in The Netherlands, the Medical Ethical Committees of participating hospitals, and from the Registration Committee of the Municipality of Amsterdam.

2.1.1. Participants

Demographic characteristics about the participating mothers and children are presented in Table 1. Attrition analysis on key variables revealed that mothers who filled in the pregnancy questionnaire and rated their child’s behaviour at age five were somewhat older (F (1,8264) = 311.42, p < .001), more often highly educated (χ² = 531.1, p < .001), had a Dutch or Western background (χ² = 583.1, p < .001) and were less anxious (F(1,7763) = 202.89, p < .001) compared to mothers who did not fill in the 5-years questionnaire.

2.2. Measurements

2.2.1. Antenatal maternal state-anxiety

Antenatal maternal state-anxiety was measured using the Dutch version of the State Trait Anxiety Inventory (STAI) [22,23] around the 16th week of gestation. This self-report questionnaire is often used to assess anxiety during pregnancy and the postnatal period [24]. The state-anxiety scale of the questionnaire consisted of 20 items scored 1–4; a higher score represents a higher level of experienced anxiety. The State-anxiety scale was found to be a valid [25] and reliable measure of temporarly or transient experienced anxiety [23]. In this study, state-anxiety scores ranged from 20 to 78 and internal consistency (Cronbach’s alpha) was .94.

2.2.2. Behavioural assessment

Children’s behaviour was reported by their mothers and primary school teachers using the Strengths and Difficulties Questionnaire (SDQ) [26]. The SDQ is a short screening questionnaire suitable for 4 to 16 year olds. The questionnaire consisted of 25 items, with positive

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Descriptive statistics of predictor, dependent variables and mother and child characteristics.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal characteristics during pregnancy Mean (SD)</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>31.8 (4.6)</td>
</tr>
<tr>
<td>Education following primary school (%)</td>
<td></td>
</tr>
<tr>
<td>0–5 years</td>
<td>13.8</td>
</tr>
<tr>
<td>6–10 years</td>
<td>35.8</td>
</tr>
<tr>
<td>11 years or more</td>
<td>50.5</td>
</tr>
<tr>
<td>Ethnicity (%)</td>
<td></td>
</tr>
<tr>
<td>Dutch</td>
<td>75.5</td>
</tr>
<tr>
<td>Turkish</td>
<td>2.6</td>
</tr>
<tr>
<td>Moroccan</td>
<td>4.0</td>
</tr>
<tr>
<td>Surinamese</td>
<td>3.5</td>
</tr>
<tr>
<td>Other western countries</td>
<td>6.6</td>
</tr>
<tr>
<td>Non-western countries</td>
<td>7.8</td>
</tr>
<tr>
<td>Smoking (%)</td>
<td>8.0</td>
</tr>
<tr>
<td>Alcohol consumption (%)</td>
<td>26.8</td>
</tr>
<tr>
<td>Nulliparous (%)</td>
<td>56.7</td>
</tr>
<tr>
<td>STAI score</td>
<td>36.7 (9.8)</td>
</tr>
<tr>
<td>STAI completed (gestational week)</td>
<td>16.3 (4.1)</td>
</tr>
<tr>
<td>Child characteristics at age 5 years</td>
<td></td>
</tr>
<tr>
<td>Gender (boy%)</td>
<td>50.3</td>
</tr>
<tr>
<td>Age (years)</td>
<td>5.1 (0.13)</td>
</tr>
<tr>
<td>Birth weight (grammes)</td>
<td>3350.3 (467.8)</td>
</tr>
<tr>
<td>SDQ mother SDQ teacher</td>
<td></td>
</tr>
<tr>
<td>Overall problem behaviour</td>
<td>5.1 (4)</td>
</tr>
<tr>
<td>Hyperactivity/inattention</td>
<td>2.4 (2.1)</td>
</tr>
<tr>
<td>Emotional symptoms</td>
<td>0.9 (1.3)***</td>
</tr>
<tr>
<td>Peer relationship problems</td>
<td>0.8 (1.2)***</td>
</tr>
<tr>
<td>Conduct problems</td>
<td>1.0 (1.2)***</td>
</tr>
<tr>
<td>Pro-social behaviour</td>
<td>8.0 (1.8)***</td>
</tr>
</tbody>
</table>

Note. SDQ = Strengths and Difficulties Questionnaire; STAI = State-Trait Anxiety Inventory.
p < .05; **p < .01; ***p < .001.
and negative statements, which are divided in 5 scales: emotional symptoms, conduct problems, hyperactivity/inattention problems, 
peer relationship problems and pro-social behaviour. All items (without pro-social behaviour items) added together form the total difficulties score that represents children’s overall problem behaviour. The SDQ has satisfactory psychometric characteristics comparable to those of the CBCL [27].

2.3. Data analysis

The association between antenatal maternal anxiety and the child’s problem behaviour was investigated using (multiple) regression in SPSS (version 17.0). Table 2 gives an overview of the bivariate correlations (parametric and non-parametric) between the independent variable (antenatal anxiety), the outcome parameters (child behaviour) and potential covariates. Risk factors (potential covariates) were chosen on a theoretical basis (literature) in the first place. Thereafter, we have tested whether a potential covariate was significantly related to the outcome variable and therefore might influence the association between antenatal anxiety and children’s problem behaviour. When a covariate was significantly related to the outcome variable of interest, it was included in the multiple regression analyses.

We assessed the potential influence of the child’s birth weight corrected for gestational age. This variable was derived from a regression model with the children’s gestational age as the predictor and their birth weight as the dependent variable. Unstandardised predicted residuals were saved and these values represent the children’s birth weight corrected for gestational age. This variable was derived from a regression model with the children’s gestational age as the predictor, maternal smoking during pregnancy (0=no/1=yes), maternal alcohol consumption during pregnancy (0=no/1=yes), maternal current emotional distress (total score of the Depression-Anxiety-Stress (DASS-21) questionnaire [28] when the child reached his or her fifth birthday), parental self-reported history of psychopathology (0=no/1=yes). Hierarchical multiple regressions with significant covariates included were performed and reported for overall problem behaviour first, followed by analyses in the behavioural subscales (Table 3).

To investigate whether the child’s sex moderated the effect of antenatal anxiety on child behaviour, interaction terms between maternal anxiety and the child’s sex were computed and tested in univariate regressions. When an interaction effect reached significance (p<.05) subsequent (multiple regression) analyses were stratified for the child’s sex.

3. Results

3.1. Cross-informant agreement

Bivariate correlations between mother and teacher ratings were r = .40 (overall problem score), r = .29 (emotional symptoms), r = .29 (conduct problems), r = .43 (hyperactivity/inattention), r = .32 (peer relationship problems), and r = .23 (pro-social behaviour) (all ps<.01).

3.2. Antenatal anxiety and children’s behaviour rated by mother

Analyses revealed a significant interaction between antenatal anxiety and the child’s sex F(1, 4372) = 4.34, p = .04, in children’s overall problem behaviour when child behaviour was rated by the mother. In boys, antenatal maternal anxiety was positively associated with the child’s overall problem behaviour F(1, 1748) = 163.2, p = .00. In girls, prenatal anxiety also showed a significant positive relation with overall problem behaviour F(1, 1724) = 128.0, p = .00, which was slightly weaker than in boys (see Fig. 1). After the addition of covariates (Table 3), antenatal maternal anxiety remained positively related to overall problem behaviour in boys and girls with stronger association in boys than in girls. Analyses revealed a significant interaction between antenatal anxiety and the child’s sex F(1, 3473) = 4.70, p = .03 in children’s hyperactivity/inattention problems. Univariate analysis showed that antenatal maternal anxiety was positively related to symptoms of hyperactivity and inattention in boys F(1, 1749) = 77.51.

Table 2

Bivariate correlations between predictor, potential covariates and dependent variables.

<table>
<thead>
<tr>
<th>SDQ Mother (N = 3446)</th>
<th>Ov prob</th>
<th>Hyp/inatt</th>
<th>Emo symp</th>
<th>Cond prob</th>
<th>Peer prob</th>
<th>Pro-social</th>
</tr>
</thead>
<tbody>
<tr>
<td>BW_GA</td>
<td>.00</td>
<td>.00</td>
<td>.00</td>
<td>.00</td>
<td>.10</td>
<td>.01</td>
</tr>
<tr>
<td>Parity</td>
<td>−.01</td>
<td>−.06**</td>
<td>−.08***</td>
<td>.03</td>
<td>.00</td>
<td>−.01</td>
</tr>
<tr>
<td>Mat age</td>
<td>−.20***</td>
<td>−.17**</td>
<td>−.11***</td>
<td>−.08***</td>
<td>−.16**</td>
<td>.00</td>
</tr>
<tr>
<td>Mat edu</td>
<td>.21</td>
<td>.27***</td>
<td>−.07***</td>
<td>−.11***</td>
<td>.21***</td>
<td>.02</td>
</tr>
<tr>
<td>Smoking</td>
<td>.08***</td>
<td>.09***</td>
<td>.00</td>
<td>.05**</td>
<td>.04**</td>
<td>.01</td>
</tr>
<tr>
<td>Alcohol</td>
<td>−.09***</td>
<td>−.06***</td>
<td>−.07***</td>
<td>−.03</td>
<td>−.12***</td>
<td>.02</td>
</tr>
<tr>
<td>Cur distr</td>
<td>.32***</td>
<td>.22***</td>
<td>.24***</td>
<td>.26***</td>
<td>.20***</td>
<td>−.10***</td>
</tr>
<tr>
<td>Par psych</td>
<td>.10***</td>
<td>.07***</td>
<td>.11***</td>
<td>.03</td>
<td>.05**</td>
<td>−.01</td>
</tr>
<tr>
<td>Anxiety</td>
<td>.28***</td>
<td>.19***</td>
<td>.15***</td>
<td>.18***</td>
<td>.24***</td>
<td>.11***</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SDQ Teacher (N = 3520)</th>
<th>Ov prob</th>
<th>Hyp/inatt</th>
<th>Emo symp</th>
<th>Cond prob</th>
<th>Peer prob</th>
<th>Pro-social</th>
</tr>
</thead>
<tbody>
<tr>
<td>BW_GA</td>
<td>−.03</td>
<td>−.04**</td>
<td>.03</td>
<td>.04</td>
<td>−.04</td>
<td>.01</td>
</tr>
<tr>
<td>Parity</td>
<td>−.01</td>
<td>−.04**</td>
<td>.03</td>
<td>.04</td>
<td>−.04</td>
<td>.01</td>
</tr>
<tr>
<td>Mat age</td>
<td>.05**</td>
<td>−.07***</td>
<td>.00</td>
<td>.04**</td>
<td>.01</td>
<td>.04</td>
</tr>
<tr>
<td>Mat edu</td>
<td>−.12***</td>
<td>−.11***</td>
<td>−.03</td>
<td>−.08***</td>
<td>−.04**</td>
<td>.04</td>
</tr>
<tr>
<td>Smoking</td>
<td>.05**</td>
<td>.06***</td>
<td>.03</td>
<td>.02</td>
<td>.01</td>
<td>.02</td>
</tr>
<tr>
<td>Alcohol</td>
<td>−.06***</td>
<td>−.04***</td>
<td>−.06***</td>
<td>−.02</td>
<td>.04**</td>
<td>.00</td>
</tr>
<tr>
<td>Cur distr</td>
<td>.09***</td>
<td>.07***</td>
<td>.06***</td>
<td>.05</td>
<td>.05</td>
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<tr>
<td>Par psych</td>
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<td>.01</td>
<td>.04</td>
<td>.00</td>
<td>.01</td>
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<tr>
<td>Anxiety</td>
<td>.10***</td>
<td>.08***</td>
<td>.06***</td>
<td>.07***</td>
<td>.06**</td>
<td>.01</td>
</tr>
</tbody>
</table>

Note. Potential covariates and predictor: BW_GA= birth weight corrected for gestational age, Mat age = maternal age, Parity: nulliparous = 0, multiparous = 1, Mat edu = maternal educational level (low, middle, high), Smoking during pregnancy: no = 0=yes = 1, Alcohol during pregnancy: no = 0=yes = 1, Cur distr = current maternal distress, Par psych = parental self-reported history of psychopathology, Anxiety = antenatal anxiety during pregnancy. Dependent variables: Ov prob = overall problem behaviour, Hyp/inatt = hyperactivity/inattention problems, Emo symp = emotional symptoms, Cond prob = conduct problems, Peer prob = peer relationship problems, Pro-social = pro-social behaviour. SDQ = Strengths and Difficulties Questionnaire. *p<.05; **p<.01; ***p<.001.

Table 3

Hierarchical multiple regression between antenatal anxiety and child problem behaviour reported by mothers and teachers.

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>β</th>
<th>R²</th>
<th>ΔR²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mother</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall problem behaviour</td>
<td>Boys</td>
<td>1654</td>
<td>.13***</td>
<td>.25***</td>
</tr>
<tr>
<td>Girls</td>
<td>1639</td>
<td>.16***</td>
<td>.26***</td>
<td>.17***</td>
</tr>
<tr>
<td>Hyperactivity/inattention</td>
<td>Boys</td>
<td>1668</td>
<td>.09***</td>
<td>13.28***</td>
</tr>
<tr>
<td>Girls</td>
<td>1659</td>
<td>.05</td>
<td>.10***</td>
<td>.09***</td>
</tr>
<tr>
<td>Emotional symptoms</td>
<td>Boys</td>
<td>3377</td>
<td>.05*</td>
<td>18.21***</td>
</tr>
<tr>
<td>Conduct problems</td>
<td>Boys</td>
<td>3308</td>
<td>.09***</td>
<td>18.58***</td>
</tr>
<tr>
<td>Girls</td>
<td>1639</td>
<td>.05</td>
<td>.10***</td>
<td>.09***</td>
</tr>
<tr>
<td>Emotional symptoms</td>
<td>Boys</td>
<td>2895</td>
<td>.04*</td>
<td>8.95***</td>
</tr>
<tr>
<td>Conduct problems</td>
<td>Boys</td>
<td>2897</td>
<td>.03</td>
<td>7.05***</td>
</tr>
<tr>
<td>Girls</td>
<td>2897</td>
<td>.03</td>
<td>7.05***</td>
<td>.03***</td>
</tr>
</tbody>
</table>

Note. β = standardised beta for antenatal anxiety only; R² = explained variance when all predictors are included in the model; ΔR² = explained variance for antenatal anxiety. Covariates included: birth weight corrected for gestational age, parity, maternal age, maternal ethnicity, maternal educational level, maternal smoking, maternal alcohol consumption, current maternal distress, parental self-reported history of psychopathology. *p<.05; **p<.01; ***p<.001.
p = .00, and in girls $F(1, 1724) = 46.33$, $p = .00$ (see Fig. 2). However, after controlling for significant covariates, antenatal anxiety remained significantly related to hyperactivity/inattention problems in boys, but not in girls. Univariate regression revealed a positive association between antenatal anxiety and children's emotional symptoms $F(1, 3475) = 76.55$, $p = .00$. After controlling for relevant covariates, antenatal anxiety remained positive but weakly related to children's emotional symptoms. Antenatal anxiety was positively related to peer relationship problems $F(1, 3475) = 215.25$, $p = .00$ in an unadjusted analysis. After covarying significant confounders, antenatal anxiety remained significantly related to peer relationship problems. A univariate regression revealed a positive relation between antenatal anxiety and children's conduct problems $F(1, 3474) = 121.32$, $p = .00$, which remained significant after controlling for significant covariates. Antenatal anxiety was negatively related to pro-social behaviour $F(1, 3467) = 39.59$, $p = .00$ in an unadjusted analysis, after covarying significant covariates this negative association remained significant.

### 3.3. Antenatal anxiety and children's behaviour rated by teacher

Univariate analysis showed significant positive relations between antenatal anxiety and children's overall problem behaviour $F(1, 3252) = 33.92$, $p = .00$, hyperactivity/inattention problems $F(1, 3254) = 21.23$, $p = .00$, emotional symptoms $F(1, 3253) = 9.73$, $p = .002$, peer relationship problems $F(1, 3254) = 18$, $p = .001$ and conduct problems $F(1, 3253) = 12.01$, $p = .001$. A significant negative association was found between antenatal anxiety and children's pro-social behaviour $F(1, 3253) = 10.04$, $p = .002$. After controlling for significant covariates (Table 3) antenatal anxiety remained positively related to children's overall problem behaviour and a negative association with pro-social behaviour was found.

### 4. Discussion

Results in the current study provided support for the hypothesis that antenatal anxiety is related to children's problem behaviour and are in accordance with a foetal programming perspective [29]. Current results corroborate findings from previous comparable studies, which have reported adverse effects of antenatal anxiety on child behaviour [5–10,19,20,30]. Children of mothers who reported higher levels of anxiety during their pregnancy showed more overall problem behaviour, hyperactivity/inattention problems, emotional symptoms, peer relationship problems, conduct problems and showed less pro-social behaviour when mothers had rated their child's behaviour. When child behaviour was rated by their primary school teachers, children showed more overall problem behaviour and less pro-social behaviour in relation with antenatal anxiety.

We found that the child's sex moderated the relation between antenatal anxiety with overall problem behaviour and hyperactivity/inattention problems in children when reported by their mother. As could be expected [31] and becomes clear from Figs. 1 and 2, baseline rates for overall problem behaviour and hyperactivity and inattention problems were higher for boys than for girls. However, Figs. 1 and 2 also show that the lines which represent boys have steeper slopes than the lines that represent girls. In other words, the lines are not parallel which suggests a moderating role of the child's sex that was confirmed by the finding of significant interaction effects in the regression models. Thus, with higher levels of antenatal anxiety, the positive association between antenatal anxiety and overall problem behaviour became stronger in boys than in girls. Furthermore, antenatal anxiety was significantly associated with hyperactivity/inattention problems in boys, while this was not the case in girls. Hence, our study corroborates the idea of sex differences in programming effects of antenatal anxiety on child behaviour in general [17] and it has provided evidence in support of our hypothesis that boys would have more overall and externalising behaviour problems [5,6,14]. On the other hand our results did not confirm our hypothesis for more emotional problems in girls born to mothers who reported higher levels of anxiety in their pregnancy [5,6,9].

A great strength of the current study was the fact that we have evaluated maternal as well as teacher reports on child behaviour separately. Cross-informant correlations were weak to moderate, which is a common finding [32]. Mothers reported their children to have more hyperactivity/inattention problems, conduct problems and to show more pro-social behaviour compared to teachers. Teachers reported more overall problem behaviour, emotional symptoms and pro-peer relationship problems.

Remarkably we found that evidence for an independent association between antenatal maternal anxiety and children's problem behaviour was most profound when mothers had reported on their child's behaviour. Literature on cross-informant discrepancies poses several possible explanations for this finding. First, as was mentioned in the introduction, mothers and teachers observe children in different circumstances where children might actually behave differently. Furthermore, mothers have known their child for a longer period of time compared to the teacher, whereas teachers in turn might be more able to view the child's behaviour in comparison with peers [11]. Second, the idea that mothers tend to over report problem behaviour (positive bias) has been studied extensively and has been linked to...
maternal psychopathology. Especially, maternal internalising symp-
tomatology (such as anxiety and depression) affects their reporting of
children's problem behaviour [13–16]. Findings in the present study
corroborate this idea as analyses showed that parental history of self-
reported psychopathology was only positively associated with maternal
reports on child behaviour. Thus, when parents had a self-reported
history of psychopathology, mothers viewed their children's behaviour
as more problematic. Teachers' evaluations of children's behaviour
(except for emotional symptoms) were not related to parental self-
reported history psychopathology. So far, previous research that was
solely based on maternal reports on child behaviour, did not take into
account this potential influence of parental history of psychopathology.
However, current results indicate that this factor influences the
association under investigation and the fact that we statistically
controlled for the influence of this variable might explain the more
modest results found in this study compared to others.

Another strength of the current study is that we were able to
statistically control for a large number of prenatal, postnatal and socio-
demographic potential risk factors in an attempt to identify the
independent influence of antenatal maternal anxiety on child behav-
ior. The choice for these covariates was primarily based on previous
studies and literature. Although to date several theoretical models (e.g.
[33]) aim to explain the association between antenatal anxiety and
children's neurodevelopment, no model specifies the strengths and
directions of the associations between all variables involved. Therefore,
results from this study that were obtained by using statistical control
for confounding factors need to be interpreted with caution. Furthermore,
the small amount of variance in children's problem behaviour that was
independently explained by antenatal maternal anxiety needs to be
taken into account while interpreting the results.

Finally, a number of important limitations need to be considered.
First, our large prospective, community based, non-clinical sample is a
clear advantage in terms of statistical power, unfortunately sample
attrition was not completely random. Women who were younger, less
well educated, who did not have a Dutch or western background, and
were more anxious during their pregnancies, were less likely to
participate in the follow-up measurements of their child. However, a
recent investigation of selective attrition in a British birth cohort has
revealed that the validity of regression models is only marginally
affected by selective attrition in large samples [34]. Second, we did not
use endocrine (e.g. cortisol) or physiological measures (e.g., heart rate
variability) and we were therefore unable to test potential underlying
mechanisms that might explain the association between maternal
anxiety and children's behavioural development. Furthermore we were
unable to rule out potential genetic factors that might affect the
association between antenatal anxiety and child behaviour problems.

A possible explanation for the fact that we did not find strong
associations could have been that the degree of antenatal anxiety
experienced by the mothers was relatively low. Their mean state-
anxiety score was 36.7 (SD = 9.8) which is equal to decile 5 in a Dutch
female norm population [23]. However, post-hoc analyses in a
subsample of highly anxious mothers (mean state-anxiety scores
above the 90th percentile) did not reveal stronger independent
associations between antenatal maternal anxiety and child behaviour.
Alternatively, mothers and teachers in the current study have reported
alternative explanation for the modest associations that were found.
Furthermore, we measured stress at only one occasion around the 16th
week of gestation. Therefore, we were unable to investigate whether
there are specifically sensitive or critical periods in pregnancy during
which the foetus is more sensitive for programming effects of maternal
anxiety. Hence, it is possible that our findings underestimated the
association under investigation and would have been stronger when
examined in other periods during pregnancy.

Despite these limitations, the current study contributed to the
existing body of literature by replicating and strengthening earlier
findings and revealing that the inclusion of multiple informants on
child behaviour is of great importance. To conclude, more research taking
sex differences in the effects of antenatal distress on behavioural develop-
ment into account is warranted in large, community based birth cohorts,
where child behaviour is assessed by multiple informants.

Conflict of interest statement
None declared.

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