Child Behavior Problems Increased by Maternal Smoking During Pregnancy

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Child Behavior Problems Increased by Maternal Smoking During Pregnancy

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ABSTRACT. We investigated the effects of maternal smoking during pregnancy on behavioral problems (i.e., not mediated by low birth weight) in 3-y-old offspring. We assessed behavioral problems in 1 377 2- to 3-y-old twin pairs (registered in the Netherlands Twin Register) with the Child Behavior Checklist for ages 2-3 y (CBCL/2-3) from Achenbach, Edelbrock, and Howell. Two to 3 y earlier (i.e., soon after the birth of the twins) we collected information about the smoking habits (i.e., “never,” “sometimes,” and “regularly”) of the mother during pregnancy. We analyzed the effect of maternal smoking on the CBCL total score and on several subscale scores for first- and second-born twins separately, and we adjusted for the possible confounding effects of birth weight, socioeconomic status, maternal age, and type of feeding (i.e., breast or bottle fed). There was a significant effect of maternal smoking on so-called “externalizing” behavioral problems (e.g., oppositional, aggressive, overactive), but not on “internalizing” behavioral problems (e.g., withdrawn, depressed, anxious), in both first- and second-born twins. The enhanced “externalizing” problems were attributed predominantly to increased aggression. Although boys have higher externalizing and aggression scores than girls, the effect of maternal smoking was the same for boys and girls.

SMOKING BY A WOMAN DURING PREGNANCY may result in pregnancy complications; a higher perinatal mortality rate; and several effects of the bodily, emotional, and intellectual development of a child. At least some of these effects are mediated by the birth-weight-reducing effect (i.e., approximately 200–250 g) of maternal smoking and, in part, by direct influences of toxic tobacco smoke constituents in organ tissue of the fetus. Low-birth-weight children, regardless of the cause, have a relatively poor prognosis with regard to physical and mental health. Although we can attribute much variation in birth weight to gestational age, the effects of maternal smoking add to the consequences for the child. Given that the birth-weight-reducing effects of maternal smoking are the same in singletons as in (individual) twins and triplets, the causative factors (i.e., decreased placental blood flow through the placental to the fetus, a nicotine-produced reduction of intrauterine partial pressure of oxygen 

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during replication and differentiation) in fetal brain and
suppressed deoxyribonucleic acid (DNA) synthesis in
the newborn brains, especially in the cerebellum.12 In a
subsequent study, identical exposure of pregnant fe-
male rats to nicotine produced in the offspring an eleva-
tion in transmitter turnover in central noradrenergic
pathways—the strongest effects being found in late-de-
veloping regions (i.e., cerebellum), intermediate effects
in earlier developing regions (i.e., cerebral cortex), and
the weakest effects in regions that mature earliest (i.e.,
midbrain and brainstem).13 Such adrenergic effects are
very likely produced by disruption of differentiation of
specific cholinergic target cells, which contain nicotine
receptors. Van de Kamp and Collins14 clearly demonstrat-
ed this effect on nicotinic receptors in mice.

Recently, Richardson and Tizabi15 presented evi-
dence of reuctions of dopaminergic activity in the off-
spring of nicotine-exposed pregnant females in the ven-
tral tegmental area (VTA), nucleus accumbens (NAcc),
and striatum (STR). The effects are typically associated
with rat hyperactive behavior.15 Furthermore, Lewis et al.16
reported that mice, bred selectively for low aggression,
had lower DNA concentrations in the NAcc and
caudate nucleus than in mice from a highly aggressive
strain.16

The observations described above are not incompat-
ible with those in children born to mothers who smoke
(i.e., increased problem behavior, hyperactivity in par-
ticular,17 poor language development, and delayed
general cognitive development18). Lanteng et al.19 posited
that being bottle fed during the first weeks of life might also be responsible for the behavioral effects
noted earlier. Mothers who smoke during pregnancy
tend to bottle feed their child; however, this action
confounds both of the above-mentioned effects.20 We
therefore investigated the prevalence of behavioral
problems in 3-y-old children (as observed by parents)
as a function of maternal smoking during pregnancy,
corrected for the confounding effects of birth weight and
breast/bottle feeding. Given that both maternal
smoking and feeding habits (i.e., breast or bottle) are
supposedly associated with social class, and because
birth weight is related to maternal age, we adjusted the
problematic behavior-smoking relationship for social
class and maternal age.

Method

Subjects. Approximately 45% of all multiple births
(mainly twins) both in the Netherlands since the end of
1986 are registered in the Netherlands Twin Register
(NTR), which is maintained by the department of phys-
iological psychology at the Free University of Ams-
tterdam. More than 9 000 twin pairs, varying in ages
between 2 mo and 8 y, have been registered, for which
parents of the children gave their written permission.
Parents complete several questionnaires about their
twins, the first of which is completed very soon after
birth, in which birth weight, gestational age, health
problems, smoking and drinking habits of the mother
during pregnancy, among others, are queried. A second
questionnaire, which is mailed to the parents when the
children are between 1.5 and 2 y of age, focuses on
health and motor development. When the children are
3 y of age, the parents complete the Child Behavior
Checklist for 2–3-y-olds (CBCL/2–3) by Achenbach,
Edelbrock, and Howe21 (translated into Dutch).22
We mailed the checklist to 1 792 families of twins, and
the families completed and returned the checklist for
1 377 twin pairs, corresponding with approximately
35% of all Dutch twins in the 2–3-y age category.

Although zygosity is not relevant for the present
study, for the sake of completeness we have provided
the numbers of each zygosity category. The total sample
of 1 377 pairs comprised 242 MZ female, 214 MZ
male, 235 DZ female, 263 DZ male, 409 male-female
pairs, and 14 pairs of unknown zygosity. The zygosity
determination procedure has been described elsewhere
by Van den Oord et al.24

Measures. Investigators use the CBCL/2–3 assessment
instrument to obtain parental ratings of problem be-
aviors in 2–3-y-old children. The list contains 99 items
that describe a large number of different behavioral
problems. Each item can be scored with 0 (not true) or
with 1 or 2 (true). The answers to the 99 items result in
scores for the following seven behavioral problem cate-
gories: (1) oppositional, (2) aggressive, (3) overactive, (4)
detected, (5) anxious, (6) sleep problems, and (7) so-
nomatic problems. The first three categories contribute
collectively to the higher-order problem category, external-
izing behavior problems, whereas withdrawn and
anxious form the higher-order category, internalizing
behavior problems. The sum of all problem categories
gives one total CBCL score.

Two to 3 y earlier (i.e., initial questionnaire mailed
shortly after birth occurred) we collected pre- and perin-
atal information, including smoking habits of the
mother during pregnancy. Three responses were provid-
ed to the question, “Did you smoke during pregnan-
cy?”: (1) never, (2) sometimes, or (3) regularly. In addi-
tion, we collected information about the following
potentially confounding factors: birth weight, socioeco-
omic status (SES [mean of scores on educational level
of father, educational level of mother, and vocational
level of father]), feeding during the first 3 wk after birth
(i.e., bottle or breast), and maternal age.

Model selection. Preliminary data analysis revealed
distributions of dependent variables (i.e., CBCL-total,
externalizing, internalizing, and all separate problem
dimensions) were highly positively skewed. To obtain a
more symmetric and nearly normal distribution, we
performed a square-root transformation on each of the
dependent variables.

For each of the dependent variables and for each child
(i.e., first or second born) separately, we used a model-fitting approach to carry out covariance analysis.
The starting point in each case was the standard covari-
ance model, with maternal smoking and sex of the child
as factors and (linear effects of) birth weight, gestation-
al age, SES, and (amount of) breast feeding as covari-
ates. We defined SES as the mean of the following vari-
ables: father’s education, mother’s education, and

16 Archives of Environmental Health
Table 1.—Effects of Maternal Smoking and Sex on Child Behavior Checklist (CBCL) Behavioral Problems With Birth Weight, Maternal Age, and Socioeconomic Status (SES) as Covariates

<table>
<thead>
<tr>
<th>Effect</th>
<th>CBCL total</th>
<th>Externalizing</th>
<th>Internalizing</th>
<th>Aggression</th>
<th>Oppositional</th>
<th>Overactive</th>
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<tbody>
<tr>
<td></td>
<td>b</td>
<td>t/F*</td>
<td>p</td>
<td>b</td>
<td>t/F*</td>
<td>p</td>
</tr>
<tr>
<td>Maternal smoking</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First born</td>
<td>.13</td>
<td>3.10</td>
<td>&lt;.005</td>
<td>.09</td>
<td>2.56</td>
<td>.01</td>
</tr>
<tr>
<td>Second born</td>
<td>.13</td>
<td>3.62</td>
<td>&lt;.001</td>
<td>.04</td>
<td>1.14</td>
<td>.26</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<td>4.32</td>
<td>&lt;.001</td>
<td>.09</td>
<td>1.62</td>
<td>.11</td>
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<tr>
<td>Second born</td>
<td>.19</td>
<td>3.45</td>
<td>&lt;.001</td>
<td>.07</td>
<td>1.66</td>
<td>.25</td>
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<tr>
<td>Maternal age</td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>First born</td>
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<td>-3.87</td>
<td>&lt;.001</td>
<td>-.05</td>
<td>-1.79</td>
<td>.07</td>
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<tr>
<td>Second born</td>
<td>-.14</td>
<td>-5.01</td>
<td>&lt;.001</td>
<td>-.09</td>
<td>-3.25</td>
<td>&lt;.005</td>
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<td>Nonsmoker</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sometimes smokes</td>
<td>-12</td>
<td>2.19</td>
<td>.03</td>
<td>-12</td>
<td>4.43</td>
<td>&lt;.001</td>
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<tr>
<td>Regularly smokes</td>
<td>-12</td>
<td>-2.31</td>
<td>.02</td>
<td>-12</td>
<td>-2.31</td>
<td>.02</td>
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<tr>
<td>Birth weight</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First born</td>
<td>-.08</td>
<td>-2.97</td>
<td>&lt;.005</td>
<td>-.03</td>
<td>-1.20</td>
<td>.23</td>
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<tr>
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<td>-2.34</td>
<td>.02</td>
<td>-.06</td>
<td>-2.22</td>
<td>.03</td>
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<td>Socioeconomic status</td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>First born</td>
<td>3.96†</td>
<td>.01</td>
<td>.01</td>
<td>6.06†</td>
<td>&lt;.001</td>
<td>.07</td>
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<tr>
<td>Nonsmoker</td>
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<td>.04</td>
<td>.06</td>
<td>-2.85</td>
<td>&lt;.005</td>
</tr>
<tr>
<td>Sometimes smokes</td>
<td>-.08</td>
<td>-2.54</td>
<td>.01</td>
<td>-.12</td>
<td>-3.97</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Regularly smokes</td>
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<td>1.10</td>
<td>.27</td>
<td>.05</td>
<td>1.51</td>
<td>.13</td>
</tr>
<tr>
<td>Second born</td>
<td>-.07</td>
<td>-2.55</td>
<td>.01</td>
<td>-.10</td>
<td>-3.22</td>
<td>&lt;.005</td>
</tr>
<tr>
<td>N</td>
<td>1226/1 224</td>
<td>1228/1 223</td>
<td>1228/1 225</td>
<td>1235/1 233</td>
<td>1228/1 227</td>
<td>1235/1 229</td>
</tr>
<tr>
<td>N</td>
<td>1.226/1 224</td>
<td>1.228/1 223</td>
<td>1.228/1 225</td>
<td>1.235/1 233</td>
<td>1.228/1 227</td>
<td>1.235/1 229</td>
</tr>
<tr>
<td>d_{eff}</td>
<td>1.217/1 218</td>
<td>1.222/1 217</td>
<td>1.219/1 219</td>
<td>1.229/1 224</td>
<td>1.222/1 221</td>
<td>1.226/1 220</td>
</tr>
<tr>
<td>t values are used, unless indicated otherwise.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
†F(3, 1 217); 
#F(3, 1 219); 
@F(3, 1 225); 
##F(3, 1 226); 
###F(3, 1 229); 
####F(3, 1 220);
profession of the father (Cronbach's $\alpha = .76$). We initially investigated in a stepwise fashion whether quadratic terms of the covariates and covariate $\times$ covariate interactions significantly improved the fit of the model. We conducted all tests at the $\alpha = .05$ level. As it turned out, no extra covariate terms were necessary. We then investigated for each covariate separately to determine whether a cell-specific term improved the model fit significantly. After we completed these two steps, we investigated whether Maternal Smoking $\times$ Sex of the Child interaction could be simplified or removed entirely. Indeed, we determined that the interaction could be removed from the model in all 12 cases. Given that breast feeding never showed a significant effect, we decided to also remove this covariate from all the models. Finally, we investigated whether effects involving maternal smoking could be described more efficiently by a linear component only.

**Results**

Of all 1,365 available mothers, 898 (65.8%) had never smoked during pregnancy, 198 (14.5%) smoked sometimes, and 269 (19.7%) smoked regularly. The results of the analyses are shown in Table 1, together with multiple correlation ($R$) and the (semi)-standardized regression coefficients ($b$) for main factors and covariates. In the case of the factorial main effects, Maternal Smoking and Sex, $b$ represents the expected increase in the standardized square-root-transformed dependent variable when the independent factor increases by one category. In the case of the (continuous) variates, $b$ represents the expected increase in the (transformed) standardized dependent variable per 1 standard deviation increase in the independent variable. In all cases, we could simply the main effect of maternal smoking by a linear component (i.e., quadratic term was not significant), but the Maternal Smoking $\times$ Covariate interactions (Table 1) were more complex. Of particular concern was the SES $\times$ Maternal Smoking interaction for CBCL total, internalizing, and overactive. One should realize that for a regression analysis with a significant Maternal Smoking $\times$ Covariate interaction, the linear main effect of Maternal Smoking must be interpreted for an average case.

One must attribute the significant smoking effect on CBCL total score to the contribution of "externalizing" to CBCL total. The effect on "internalizing" was much weaker or negligible. The CBCL total was more significantly elevated in boys than girls, and this is attributed to the enhanced (constituting) externalizing score. Maternal smoking, which was also associated significantly with CBCL total, resulted from the increased externalizing score for children of mothers who smoked. Internalizing in boys was not different from that in girls. Given that externalizing is the important second-order CBCL factor associated with maternal smoking, we analyzed more specifically the constituting first-order factors (i.e., oppositional, aggressive, and overactive). The results, which are shown in Table 1, indicate a very significant effect of sex (i.e., boys scoring higher than girls for aggressive and overactive and, in first-born twins only, oppositional, all of which confirm earlier research.$^{23,25}$ Furthermore, all problem categories that constitute externalizing were associated positively and particularly with maternal smoking, aggressive, and oppositional behaviors.

We also noted what appeared to be significant interactions between maternal smoking and SES for some of the problem categories (Table 1).

**Discussion**

The results of the present study suggested that toxic tobacco smoke constituents—most likely nicotine—that circulate in maternal blood may pass through the placenta and enter into the fetal circulation. At this point, they can pass the fetal blood-brain barrier and affect tissue of the central nervous system. Perhaps that was the reason for increase CBCL problem-behavior scores (particularly aggressive and overactive scores) in children born to mothers who smoked. We realize that our data did not allow us to draw this conclusion directly. First, our experimental design did not allow us to infer causality. Animal experimental evidence, however, as cited in the introduction herein, provides proof that nicotine administered to pregnant animals arrives at several sites of the central nervous system of the offspring and leads to behavioral effects comparable to human externalizing types of behavior. One should realize that aggressive people tend to smoke and that smoking mothers may pass this behavioral feature to their offspring, as is the case with other personality traits. Such a mechanism could produce the results mentioned earlier. Apart from the animal data, which point to a causal relationship, another argument against the genetic explanation originates from the observation that smoking behavior and hostility (assuming that they is strongly related to aggression) are correlated for reasons of shared environmental influences and not because common genes exist.$^{23}$

The incidental interactions between SES and maternal smoking suggest that the effect of smoking on problem behavior(s) is smaller in higher SES categories. In conclusion, the results of the present study showed that maternal smoking during pregnancy has adverse effects on later behavior(s) of children. In particular, externalizing behavior problems appear to be increased. We suggest maternal smoking might directly affect structures in the central nervous system, in turn leading to enhanced externalizing behavior (specifically aggression) in the offspring.

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References