Archives of Environmental Health: An International Journal

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/vzeh20

Child Behavior Problems Increased by Maternal Smoking During Pregnancy

Jacob F. Orlebeke [a] , Dirk L. Knol [a] & Frank C. Verhulst [b]

[a] Vrije Universiteit, Department of Physiological Psychology Amsterdam, The Netherlands

[b] Sophia Children's Hospital Rotterdam, The Netherlands

Available online: 05 Apr 2010

To cite this article: Jacob F. Orlebeke, Dirk L. Knol & Frank C. Verhulst (1999): Child Behavior Problems Increased by Maternal Smoking During Pregnancy, Archives of Environmental Health: An International Journal, 54:1, 15-19

To link to this article: http://dx.doi.org/10.1080/00039899909602231

Child Behavior Problems Increased by Maternal Smoking During Pregnancy

JACOB F. ORLEBEKE
DIRK L. KNOL
Vrije Universiteit
Department of Physiological Psychology Amsterdam
The Netherlands

FRANK C. VERHULST
Sophia Children's Hospital Rotterdam
The Netherlands

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behavioral problems (e.g., oppositional, aggressive, overactive), but not on "internalizing" behavioral problems (e.g., withdrawn, depressed, anxious), in both first- and second-born twins.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 on the bodily, emotional, and intellectual development of a child.[1,2] At least some of these effects are mediated by the birth-weight-reducing effect (i.e., approximately 200–250 g[3,4]) 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.[5,6] 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,[7,8] 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 [pO_2], and carbon-monoxide [CO] -produced decreased O_2 supply to fetus) must be located in the mother and not in the individual children.

One must nevertheless assume that toxic tobacco smoke constituents are also transported to the child. The results of several experimental animal studies indicate that exposition of adult female animals during pregnancy has measurable neurophysiological and neuroanatomical effects in the offspring. Peters[9] determined in rats that 6 mg nicotine per kg/d (given in drinking water throughout pregnancy) increased adrenergic receptor binding significantly in the cerebral cortex of adult male offspring. The receptor binding appears to involve only α^1-receptors—and not α^2 or β subtype receptors.[10,11]

Intravenous injection of 6 mg/kg · d nicotine to adult female rats during the first 20 d of gestation resulted in elevated activity of the enzyme ornithine decarboxylase (ODC; this enzyme and its metabolites [the polyamines] are the major regulators of macromolecule synthesis

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 female rats to nicotine produced in the offspring an elevation in transmitter turnover in central noradrenergic pathways—the strongest effects being found in late-developing 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 Collins[14] clearly demonstrated this effect on nicotinic receptors in mice.

Recently, Richardson and Tizabi[15] presented evidence of reuctions of dopaminergic activity in the offspring of nicotine-exposed pregnant females in the ventral 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 incompatible with those in children born to mothers who smoke (i.e., increased problem behavior, hyperactivity in particular,[17] poor language development, and delayed general cognitive development[18]). 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 physiological psychology at the Free University of Amsterdam. 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 Howell[21,22] (translated into Dutch[23]). 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 behaviors 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 categories: (1) oppositional, (2) aggressive, (3) overactive, (4) withdrawn, (5) anxious, (6) sleep problems, and (7) somatic problems. The first three categories contribute collectively to the higher-order problem category, externalizing 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 perinatal information, including smoking habits of the mother during pregnancy. Three responses were provided to the question, "Did you smoke during pregnancy?": (1) never, (2) sometimes, or (3) regularly. In addition, we collected information about the following potentially confounding factors: birth weight, socioeconomic 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 covariance model, with maternal smoking and sex of the child as factors and (linear effects of) birth weight, gestational age, SES, and (amount of) breast feeding as covariates. We defined SES as the mean of the following variables: father's education, mother's education, and

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

Effect	CBCL total			Externalizing			Internalizing			Aggression			Oppositional			Overactive		
	b	*t/F**	*p*	*b*	*t/F*	*p*	*b*	*t/F*	*p*	*b*	*t/F*	*p*	*b*	*t/F*	*p*	*b*	*t/F*	*p*
Maternal smoking																		
First born	.13	3.10	<.005	.09	2.56	.01	.07	2.00	.05	.08	2.37	.02	.09	2.42	.02	.09	2.14	.03
Second born	.13	3.62	<.001	.13	3.69	<.001	.04	1.14	.26	.13	3.43	<.001	.13	3.56	<.001	.12	2.73	.005
Sex																		
First born	.24	4.32	<.001	.27	4.89	<.001	.09	1.62	.11	.49	8.93	<.001	.13	2.26	.02	.26	4.60	<.001
Second born	.19	3.45	<.001	.22	3.87	<.001	.07	1.16	.25	.46	8.48	<.001	.05	0.91	.37	.22	3.97	<.001
Maternal age																		
First born	−.11	−3.87	<.001	−.13	−4.39	<.001	−.05	−1.79	.07	−.13	−4.64	<.001	−.09	−3.16	<.005	−.14	−4.76	<.001
Second born	−.14	−5.01	<.001	−.15	−5.13	<.001	−.09	−.325	<.005		9.70§	<.001	−.11	−3.89	<.001	−.17	−5.87	<.001
Nonsmoker										−.06	−2.19	.03						
Sometimes smokes										−.12	−4.43	<.001						
Regularly smokes										−.06	−2.31	.02						
Birth weight																		
First born	−.08	−2.97	<.005	−.10	−3.46	<.001	−.03	−1.20	.23	−.06	−2.16	.03	−.10	−3.52	<.001	−.08	−2.76	.005
Second born	−.07	−2.34	.02	−.06	−2.22	.03	−.00	−0.11	.91	−.05	−1.73	.08	−.04	−1.50	.13	−.07	−2.55	.01
Socioeconomic status																		
First born		3.96†	.01	−.08	−2.17	.01		6.06‡	<.001	−.08	−2.85	<.005	−.07	−2.23	.03		5.79//	<.001
Nonsmoker	−.06	−2.05	.04				.00	0.07	.94							−.09	−3.03	<.005
Sometimes smokes	−.08	−2.54	.01				−.12	−3.97	<.001							−.06	−2.06	.39
Regularly smokes	.04	1.10	.27				.05	1.51	.13							.06	1.94	.52
Second born	−.07	−2.55	.01	−.06	−2.18	.03	−.10	−3.22	<.005	−.04	−1.50	.13	−.04	−1.41	.16		4.43#	<.005
Nonsmoker																−.09	−3.34	<.001
Sometimes smokes																−.03	−0.97	.33
Regularly smokes																.04	1.06	.29
First/second born																		
N	1 226/1 224			1 228/1 223			1 228/1 225			1 235/1 233			1 228/1 227			1 235/1 229		
R	.24/.25			.25/.25			.15/.16			.31/.31			.20/.19			.24/.26		
df_{error}	1 217/1 218			1 222/1 217			1 219/1 219			1 229/1 224			1 222/1 221			1 226/1 220		

*t values are used, unless indicated otherwise.
†*F*(3, 1 217).
‡*F*(3, 1 219).
§*F*(3, 1 225).
//*F*(3, 1 226).
#*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 × 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 × 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 × Covariate interactions (Table 1) were more complex. Of particular concern was the SES × Maternal Smoking interaction for CBCL total, internalizing, and overactive. One should realize that for a regression analysis with a significant Maternal Smoking × 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.[25]

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.

* * * * * * * * * *

Submitted for publication July 18, 1996; revised; accepted for publication April 2, 1998.

Requests for reprints should be sent to Jacob F. Orlebeke, Free University, Department of Physiological Psychology, De Boelelaan 1111, 1081 HV Amsterdam, The Netherlands.

* * * * * * * * * *

References

1. Nasrat HA, Al-Hachim GM, Mahmoud FA. Perinatal effects of nicotine. Biol Neonate 1986; 49:8–14.
2. Butler NR, Goldstein A. Smoking in pregnancy and subsequent child development. Br Med J 1973; 4:573–75.
3. Simpson WJ. A preliminary report on cigarette smoking and the incidence of prematurity. Am J Obstet Gynecol 1957; 73:808–15.
4. Brooke OG, Anderson HR, Bland JM, et al. Effects on birth weight of smoking, alcohol, caffeine, socioeconomic factors, and psychosocial stress. Br Med J 1989; 298:795–801.
5. McCormick MC, Gortmaker SL, Sobol AM. Very low birth weight children: behavior problems and school difficulty in a national sample. J Pediat 1990; 117:687–93.
6. Veen S, Ens-Dokkum MH, Schreuder AM, et al. Impairments, disabilities, and handicaps of very preterm and very-low-birth-weight infants at five years of age. Lancet 1991; 338:33–36.
7. Orlebeke JF, Boomsma DI, Eriksson AW. Epidemiological and birth weight characteristics of triplets: a study from the Dutch Twin Register. Europ J Obstet Gynecol Repro Biol 1993; 50:87–93.
8. Orlebeke JF, Boomsma DI, Van Baal GCM, et al. Effect of maternal smoking on birth weight of twins: a study from the Dutch Twin Registry. Early Human Develop 1994; 37:161–66.
9. Peters DAV. Prenatal nicotine exposure increases adrenergic receptor binding in the rat cerebral cortex. Res Commun Chem Pathol Pharmacol 1984; 46:307–17.
10. Navarro HA, Mills E, Seidler FJ, et al. Prenatal nicotine exposure impairs β-adrenergic function: persistent chronotropic sensitivity despite recovery from deficits in receptor binding. Brain Res Bull 1990a; 25:233–37.
11. Navarro HA, Slotkin TA, Tayyeb MI, et al. Effects of fetal nicotine exposure on development of adrenergic receptor binding in rat brain regions: selective changes in α1-receptors. Res Commun Substance Abuse 1990b; 11:95–103.
12. Slotkin TA, Greer N, Faust J, et al. Effects of maternal nicotine injections on brain development in the rat: ornithine decarboxylase activity, nucleic acids and proteins in discrete brain regions. Brain Res Bullet 1986; 17:41–50.
13. Slotkin TA, Cho H, Whitmore WL. Effects of prenatal nicotine exposure on neuronal development: selective actions on central and peripheral catecholaminergic pathways. Brain Res Bull 1987; 18:601–11.
14. Van de Kamp J, Collins AC. Prenatal nicotine alters nicotine receptor development in the mouse brain. Pharmacol Biochem Behavior 1994; 47:889–900.
15. Richardson SA, Yizabi Y. Hyperactivity in the offspring of nicotine-treated rats: role of the mesolimbic and nigrostriatal dopaminergic pathways. Pharmcol Biochem Behavior 1993; 47:331–37.
16. Lewis MH, Gariépy JL, Gendreau MS, et al. Social reactivity in D_1 dopamine receptors: studies in mice selective bred for high and low levels of aggression. Neuropsychopharmacol 1994; 10: 115–22.
17. Weitzman M, Gortmaker S, Sobol A. Maternal smoking and behavior problems of children. Pediatr 1992; 90:342–49.
18. Sexton M, Lynn FN, Heber JR. Prenatal exposure to tobacco. II. Effects on cognitive functioning at age three. Intern J Epidemiol 1990;19:72–77.
19. Lanting CI, Fidler V, Huisman M, et al. Neurological differences between 9-year-old children fed breast milk or formula milk as babies. Lancet 1994; 344:1319–22.
20. Orlebeke JF, Stroet TM, Boomsma DI. Breastfeeding and neurological status. Lancet 1995; 345:393.
21. Achenbach TM, Edelbrock C, Howell CT. Empirically based assessment of the behavioral/emotional problems of 2- and 3-year-old children. J Abnorm Child Psychol 1987; 15:629–50.
22. Achenbach TM. Manual for the Child Behavior Checklist and 1991 Profile. Burlington, VT: University of Vermont, 1991.
23. Koot H. Problem Behavior in Dutch Preschoolers. Dissertation Erasmus University. Rotterdam, the Netherlands: ISBN 90-9006482-6.
24. Van den Oord EJCG, Koot HM, Boomsma DI, et al. A twin-singleton comparison of problem behavior in 2–3-year-olds. J Child Psychol Psychiatr 1995; 36:449–58.
25. Kaprio J, Boomsma DI, Heikkilä K, et al. Genetic variation in behavioral risk factors for atherosclerosis: twin-family study in smoking and cynical hostility. Atherosclerosis 1995; 10:634–37.