

TOBACCO AND PREGNANCY

[Archived] Tobacco Consumption During Pregnancy and Its Impact on Child Development

David Fergusson, PhD

Christchurch School of Medicine, New Zealand

June 2002

Introduction

Over the past decade, increasingly more research has been conducted regarding the statistical linkages between mothers who smoke during pregnancy and the development of externalizing behaviours¹⁻¹⁰ in their children, such as conduct problems, hyperactivity and crime.

Subject

Most of this research has been focussed on:

- a. examining statistical linkages between prenatal tobacco exposure and postnatal adjustments; and
- b. adjusting these associations to take confounding factors into consideration. Research into human populations has been supplemented by animal studies that examine the effects of

prenatal nicotine exposure on subsequent postnatal behaviour in offspring.¹¹

Problems

The key problems in this area of investigation are as follows:

- a. establishing that prenatal tobacco exposure makes a unique and causal contribution to subsequent behavioural adjustment in offspring; and
- b. determining the underlying mechanisms and processes by which prenatal tobacco exposure may lead to an increased susceptibility to problem behaviour.

Research Context

Most of the studies that have examined this issue use longitudinal designs of rates of externalizing behaviours to permit comparisons between the offspring of smokers and the offspring of non-smokers. In addition, most studies include statistical control for a range of individual, family, and social confounding factors. Human studies have been supplemented by laboratory-based animal experiments that have examined the effects of nicotine exposure during pregnancy on the subsequent behavioural and neurophysiological functioning of rats, mice and guinea pigs.

Key Research Questions

The key research questions in this area are as follows:

- a. Does prenatal tobacco exposure increase the rates of subsequent behavioural problems, hyperactivity and crime in offspring? and
- b. If exposure to prenatal tobacco exposure has a causal linkage to increased rates of problem behaviours, what underlying mechanisms explain this association?

Recent Research Results

a) Human Studies

A growing number of studies have examined the linkages between prenatal exposure to smoking and subsequent adjustment in childhood, adolescence and young adulthood.¹⁻¹⁰ Overall, these studies suggest three generalizations about the linkages between prenatal exposure and the subsequent behavioural adjustment of offspring:¹³

1. **Association:** There is generally consistent evidence to suggest that increased prenatal exposure to smoking is associated with higher rates of conduct problems, hyperactivity and juvenile crime in offspring. These associations have been found in childhood,¹⁻³ adolescence⁴⁻⁷ and adulthood.⁸⁻¹⁰
2. **Confounding:** Although studies vary in the degree to which they control for confounding factors,¹¹ the associations between prenatal tobacco exposure and subsequent adjustment in children have been found to persist after controls were applied for a wide range of individual, family and social factors associated with smoking during pregnancy.¹¹⁻¹³ These controls allowed researchers to isolate the postnatal impact of prenatal tobacco exposure from factors that heighten the maternal propensity to smoke during pregnancy.
3. **Specificity of Association:** Although studies have been able to show consistent linkages with externalizing behaviours in offspring (such as conduct problems, hyperactivity and crime), prenatal tobacco exposure has been found to be unrelated to other aspects of personal adjustment, including internalizing disorders and other mental health problems.^{17,14}

b) Animal Studies

Many studies have examined the effects of prenatal nicotine exposure on post-natal behaviour in rats, mice and guinea pigs.¹⁵⁻¹⁷ These studies have the advantage of using precisely calibrated measures of exposure to nicotine and ensuring that this exposure is unrelated to confounding factors.¹¹ The difficulty in animal studies lies in measuring outcomes that are analogous to externalizing behaviours in humans. Nonetheless, animal studies have found that prenatal exposure to nicotine is associated with higher levels of locomotor activity.¹⁵⁻¹⁷ In addition, recent research has suggested that prenatal exposure to smoking may be linked to both structural and functional changes in the foetal brain.¹¹ However, the extent to which such changes may explain further linkages between prenatal exposure to smoking and externalizing behaviours in humans remains unclear.¹¹

Conclusions

Human studies have established a consistent and replicable association between prenatal tobacco exposure and postnatal antisocial behaviours. This association is resilient to controls for confounding. Although this evidence is generally consistent with the hypothesis that prenatal nicotine exposure leads to an increased risk of subsequent antisocial behaviour in offspring, it would be unwise to draw any firm conclusions on the basis of the current body of evidence. There

are several important issues that need to be addressed before such conclusions may be drawn. These issues include:

a) Genetic Confounding

Although existing studies have now controlled for a relatively wide range of confounding social and environmental factors, an important source of uncontrolled confounding involves genetic factors. It could be suggested that the association between prenatal tobacco exposure and post-natal adjustment problems reflects a genetic process in which the children of mothers who smoke during pregnancy are more likely to inherit genotypes that are associated with an increased risk of subsequent externalizing behaviours. Two lines of evidence support this conjecture. First, there is a known association between cigarette smoking and antisocial behaviours,¹⁸⁻¹⁹ thereby implying that mothers who smoke during pregnancy may be more prone to antisocial behaviours. Second, it is also known that the heritability of antisocial behaviours is significantly high.²⁰⁻²¹ To understand the linkages between smoking during pregnancy and antisocial behaviours, we must find ways and means of examining the role of genetic factors.

b) Identification of Underlying Mechanisms

We could more easily interpret evidence from epidemiological studies by identifying the underlying biological linkages between prenatal tobacco exposure and the development of antisocial behaviour. There are a variety of suggestions about underlying mechanisms present in such cases, including: foetal hypoxia; changes in serotonin uptake; changes in dopaminergic systems; and changes in DNA and RNA synthesis in the brain.^{2,3,6,11} However, these accounts remain highly speculative.

Given the ambiguities in the evidence noted above, perhaps the most prudent way to sum up the research in this area is to say that *smoking during pregnancy may be related to increased risks of long-term externalizing behaviours in children, but that the origins of this relationship and the extent to which statistical associations reflect causal processes remain highly uncertain.*

Implications on Policy and Service Development

Apart from the current research on a possible causal linkage between prenatal tobacco exposure and increased subsequent susceptibility to externalizing behaviours in offspring, there is an abundance of well-established epidemiological evidence to support public health initiatives in

reducing and, ideally, eliminating smoking during pregnancy. This evidence includes increased risk of spontaneous abortion,²² reduced birth weight,^{23,24} compromised perinatal status,²³ and reduced intelligence.²⁵ Therefore, from a policy and service development perspective, the findings we have discussed (suggesting that prenatal tobacco exposure may contribute to subsequent antisocial behaviours) add another dimension to arguments about the detrimental effects of smoking during pregnancy. While it would be premature to infer that prenatal exposure to cigarette smoke may be the cause for subsequent externalizing behaviours, it would be equally premature to discount this possibility. The results of current research suggest that, in future, increased risks of antisocial behaviour may be added to the growing list of adverse consequences of smoking during pregnancy.

References

1. Weitzman M, Gortmaker S, Sobol A. Maternal smoking and behavior problems of children. *Pediatrics* 1992;90(3):342-349.
2. Fergusson DM, Horwood LJ, Lynskey MT. Maternal smoking before and after pregnancy: effects on behavioral outcomes in middle childhood. *Pediatrics* 1993;92(6):815-822.
3. Millberger S, Biederman J, Faraone SV, Chen L, Jones J. Is maternal smoking during pregnancy a risk factor for attention deficit hyperactivity disorder in children? *American Journal of Psychiatry* 1996;153(9):1138-1142.
4. Rantakallio P. A follow-up study up to the age of 14 of children whose mothers smoked during pregnancy. *Acta Paediatrica Scandinavica* 1983;72(5):747-753.
5. Rantakallio P, Laara E, Isohanni M, Moilanen I. Maternal smoking during pregnancy and delinquency of the offspring: an association without causation? *International Journal of Epidemiology* 1992;21(6):1106-1113.
6. Wakschlag LS, Lahey BB, Loeber R, Green SM, Gordon RA, Leventhal BL. Maternal smoking during pregnancy and the risk of conduct disorder in boys. *Archives of General Psychiatry* 1997;54(7):670-676.
7. Fergusson DM, Woodward LJ, Horwood LJ. Maternal smoking during pregnancy and psychiatric adjustment in late adolescence. *Archives of General Psychiatry* 1998;55(8):721-727.
8. Brennan PA, Grekin ER, Mednick SA. Maternal smoking during pregnancy and adult male criminal outcomes. *Archives of General Psychiatry* 1999;56(3):215-219.
9. Weissman MM, Warner V, Wickramaratne PJ, Kandel DB. Maternal smoking during pregnancy and psychopathology in offspring followed to adulthood. *Journal of the American Academy of Child and Adolescent Psychiatry* 1999;38(7):892-899.
10. Rasanen P, Hakko H, Isohanni M, Hodgins S, Jarvelin MR, Tiihonen J. Maternal smoking during pregnancy and risk of criminal behavior among adult male offspring in the Northern Finland 1966 birth cohort. *American Journal of Psychiatry* 1999;156(6):857-862.
11. Ernst M, Moolchan ET, Robinson ML. Behavioral and neural consequences of prenatal exposure to nicotine. *Journal of the American Academy of Child and Adolescent Psychiatry* 2001;40(6):630-641.
12. Fergusson DM. Prenatal smoking and antisocial behavior. *Archives of General Psychiatry* 1999;56(3):223-224.

13. Eskenazi B, Castorina R. Association of prenatal maternal or postnatal child environmental tobacco smoke exposure and neurodevelopmental and behavioral problems in children. *Environmental Health Perspectives* 1999;107(12):991-1000.
14. Orlebeke JF, Knol DL, Verhulst FC. Child behavior problems increased by maternal smoking during pregnancy. *Archives of Environmental Health* 1999;54(1):15-19.
15. Ajarem JS, Ahmad M. Prenatal nicotine exposure modifies behavior of mice through early development. *Pharmacology Biochemistry and Behavior* 1998;59(2):313-318.
16. Johns JM, Louis TM, Becker RF, Means LW. Behavioral effects of prenatal exposure to nicotine in guinea pigs. *Neurobehavioral Toxicology and Teratology* 1982;4(3):365-369.
17. Richardson SA, Tizabi Y. Hyperactivity in the offspring of nicotine treated-rats: role of the mesolimbic and nigrostriatal dopaminergic pathways. *Pharmacology Biochemistry and Behavior* 1994;47(2):331-337.
18. Hawkins JD, Catalano RF, Miller JY. Risk and protective factors for alcohol and other drug problems in adolescence and early adulthood: Implications for substance abuse prevention. *Psychological Bulletin* 1992;112(1):64-105.
19. Kandel DB. Drug and drinking behavior among youth. *Annual Review of Sociology* 1980;6:235-285.
20. Rutter M, Macdonald H, Le Courteur A, Harrington R, Bolton P, Bailey A. Genetic factors in child psychiatric disorders -II. Empirical findings. *Journal of Child Psychology & Psychiatry & Allied Disciplines* 1990;31(1):39-83.
21. Eaves LJ, Silberg JL, Meyer JM, Maes HH, Simonoff E, Pickles A, Rutter M, Neale MC, Reynolds CA, Erikson MT, Heath AC, Loeber R, Truett KR, Hewitt JK. Genetics and developmental psychopathology: 2. The main effects of genes and environment on behavioral problems in the Virginia Twin Study of Adolescent Behavioral Development. *Journal of Child Psychology & Psychiatry & Allied Disciplines* 1997;38(8):965-980.
22. Kline J, Stein ZA, Susser M, Warburton D. Smoking: a risk factor for spontaneous abortion. *New England Journal of Medicine* 1977;297(15):793-796.
23. Kramer MS. Intrauterine growth and gestational duration determinants. *Pediatrics* 1987;80(4):502-511.
24. English PB, Eskenazi B. Reinterpreting the effects of maternal smoking on infant birthweight and perinatal mortality: A multivariate approach to birthweight standardization. *International Journal of Epidemiology* 1992;21(6):1097-1105.
25. Naeye RL, Peters EC. Mental development of children whose mothers smoked during pregnancy. *Obstetrics & Gynecology* 1984;64(5):601-607.