

**EFFECTS OF PERINATAL EXPOSURE TO ENVIRONMENTALLY
PERSISTENT ORGANIC POLLUTANTS AND HEAVY METALS ON
NEUROBEHAVIORAL DEVELOPMENT IN JAPANESE CHILDREN: III.
MATERNAL SMOKING CONFOUNDS NEONATAL
NEUROBEHAVIORAL STATUS**

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Introduction

From several epidemiological studies, it has been reported that there are some associations between perinatal exposures to PCBs, dioxins and heavy metals and neurobehavioral defects such as postnatal growth delay and poorer cognitive function. In this study, we designed a prospective cohort study to examine the effects of perinatal exposures to environmentally persistent organic pollutants on neurobehavioral development in Japanese children. This report showed some preliminary data regarding the results of the Neonatal Behavioral Assessment Scales (NBAS), in which we examined the effect of maternal smoking during pregnancy as the confounding factor to the infant neurobehavioral development.

Maternal smoking is well known to have various influences on birth outcome and growth parameters. Children of smoking mothers are often born with a lower birth weight than expected for gestational age. In addition, there is an increased chance of premature labour, intrauterine growth retardation, and perinatal mortality. Recently, the concern on the effects on the neurobehavioral development has been also increased. In studies of the effects of teratogens, NBAS has been recommended and is commonly used as a measure of central nervous system (CNS) development in the neonates. Several investigators have reported that prenatal exposure to tobacco adversely affects CNS development, as measured by the NBAS. Even though, there is no report on this association in Japan.

Methods and Materials

Three hundred forty-four pregnant healthy women attending two obstetrics clinics in Sendai gave their consents to participate in this study according to guidelines established by the ethical committee established by the Tohoku University Graduate School of Medicine. The mean age at the time of delivery was 31.85 (SD 4.69). Women were asked about tobacco use before and during

pregnancy. They were then classified as Nonsmokers, Ex-smokers and Smokers; the women who ceased to smoke prior to or throughout pregnancy were defined as the Ex-smokers. Information was obtained about pregnancy, labour, and delivery conditions from their medical records.

The NBAS was administrated at three days of after birth to 344 (179 boys and 165 girls) infants. They were all singleton and full-term (37 to 42 weeks) infants. In addition, their birth weight was 2500g or more. Examiners of the NBAS were trained and certified to administer the NBAS at the Training Center for NBAS in the Nagasaki University School of Medicine in Japan. Reliability checks were conducted throughout data collection to maintain a 90% level of agreement. Examiners were unaware of the exposure status of the infants including the maternal use of tobacco.

In statistical analysis, comparison between groups of continuous demographic, health, and growth outcomes were performed with ANOVA. For the comparison of categorical variables such as sex and parity were performed using Fisher's exact test. Analyses controlling for maternal age at the time of delivery, sex, Apgar scores, gestational age, birth weight, length and head circumference were performed using a multiple regression analysis.

Results and Discussion

Twelve (3.4%) of 344 mothers smoked an average of 13.0 (SD 6.5) cigarettes per day during pregnancy. Of 332 mothers who did not smoke, 44 were Ex-smokers and 288 were Nonsmokers. There was a significant difference between the infants of smoking and nonsmoking mothers in maternal age at the time of delivery, but no differences in gestational age, Apgar scores, birth weight, length, and head circumference were observed (Table 1).

Table 1 Maternal and infant characteristics

	Maternal smoking during pregnancy		
	No		Yes
	Nonsmoker (n=288)	Ex-smoker (n=44)	Smoker (n=12)
Maternal age*	32.2 (4.3)	30.4 (6.0)	29.1 (4.3)
¹⁾ Sex (M/F)	145/143	28/16	6/6
¹⁾ Parity (first/other)	144/144	30/14	6/6
Apgar 1min	8.0 (0.9)	7.9 (0.7)	8.3 (0.5)
Gestational age (weeks)	39.4 (1.4)	39.7 (1.3)	39.2 (1.4)
Birth weight (g)	3018 (378)	3108 (380)	3184 (415)
Birth length (cm)	48.9 (2.2)	49.3 (1.3)	49.0 (2.1)
Head circumference (cm)	33.5 (1.4)	33.4 (1.3)	33.9 (1.4)

ANOVA

Mean (SD)

¹⁾ Fisher's exact test

* P<0.05

There were no significant differences among three groups on any of the seven NBAS cluster scores. When the scores of the 28 behavioral items of the NBAS were examined, the infants of Smokers were significantly poorer than those of Ex-smokers and Nonsmoker on the three items, "General tone", "Peak of excitement" and "Cuddliness" (Table 2). These three items remained to be significant after controlling for maternal age at the time of delivery, sex, Apgar scores, gestational age, birth weight, length, and head circumference.

Table 2 NBAS scores

	Maternal smoking during pregnancy		
	No		Yes
	Nonsmoker	Ex-smoker	Smoker
General tone* (<i>MOTOR cluster</i>)	4.5 (1.3) n=236	5.2 (1.6) n=42	4.4 (2.1) n=9
Peak of excitement* (<i>RANGE OF STATE cluster</i>)	5.1 (1.0) n=254	4.9 (1.0) n=43	4.4 (1.1) n=11
Cuddliness* (<i>REGULATION OF STATE cluster</i>)	4.6 (1.3) n=254	4.8 (1.8) n=43	3.6 (1.5) n=11

ANOVA

Mean (SD)

* P<0.05

Using blinded developmental examinations, and adjusting for other factors, we observed some neurobehavioral defects in infants exposed to tobacco. This result indicates that maternal smoking during the pregnancy is an important risk factor in the infant's neurobehavioral development, and therefore, maternal smoking is confirmed to be a significant confounding factor to consider the effect of perinatal exposures to PCBs, dioxins, and heavy metals on neurobehavioral development. In the literatures, maternal smoking during pregnancy is well known to affect neurobehavioral development, but this is the first report to demonstrate this association in Japanese children. Although this study is not originally designed in order to clarify the risks of maternal smoking, the results might be important to consider the smoking of pregnant women in Japan. Several studies have recently found the reduction in IQ scores in children born to women who smoked during pregnancy. This report represents one of our prospective cohort study to examine the perinatal exposures to environmentally persistent organic pollutants and heavy metals on neurobehavioral development. The long-term effects on child neurocognitive functioning such as IQ should be also clarified in our cohort study.

The present results showed not only that maternal smoking could be a potent confounding factor to examine the effect of perinatal exposures to PCBs, dioxins, and heavy metals to

neurobehavioral development, but also that our NBAS seemed to be enough sensitive to detect a small defects potentially present in the infants exposed to the pollutants.

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